CHAPTER IV

Factors Influencing the Incidence of Wound Infection

IT IS FUNDAMENTAL in surgery that the development of an infection in a surgical wound is determined by the interaction of several forces: the nature and degree of bacterial contamination of the wound, local tissue features of the operative wound itself, and the general resistance of the patient, perhaps modified by therapeutic measures. Although this is widely accepted, there are few indications of the relative importance of these factors, and there is no unanimity as to what features of local tissue resistance or general host resistance are dominant in preventiing wound infection.

It was believed during the planning of this study that exact characterization of both patient and operation, according to pre-established standards, would be of value not only in analyzing the efficacy of ultraviolet irradiation but also in generating information that might indicate what operative and patient factors are important in the development of wound infection. Examination of the data confirmed that belief.

Various characteristics of the patient, the operation, and the pre- and postoperative course are considered in this chapter in relation to the development of wound infection. For some factors there is a positive correlation with the incidence of wound infection; for other factors no such correlation can be demonstrated. Where an apparent relationship between a given factor and wound infection rate has been observed, that factor is examined statistically in more detail to determine whether the relationship is due exclusively to the factor under consideration or to other associated variables.

This chapter considers first ultraviolet irradiation of the operating room and type of operation, then (not in this order) bacterial contamination, patient age, metabolic and nutritional factors, existence of other infections, duration of operation, and duration of preoperative hospitalization (all shown to have a major relationship to wound infection); race (minor relationship); wound drainage and administration of prophylactic antibiotics (possible relationship); and sex, wound closure, urgency, time, and date of operation (no relationship).

Ultraviolet Irradiation of the Operating Room

Previous reports on the use of ultraviolet irradiation in operating rooms to reduce the incidence of postoperative wound infection are summarized in Chapter II. Although striking benefits have been reported, few hospitals have installed ultraviolet lamps in their operating rooms. The reason for this apparent lack of acceptance, perhaps overconfidence in antibiotics or doubts concerning the validity of tests using only retrospective controls, can only be conjectured. But if direct irradiation of the operating room can substantially reduce the incidence of infection in clean operative wounds, then a valuable surgical tool is being overlooked. The purpose of this section is to re-examine the effects of direct ultraviolet irradiation of operating rooms.

The design and method of conduct of the study are described in detail in Chapter III. However, certain aspects of the study which are particularly important to the validity of the evaluation will bear repeat-

ing. Each operating room used in the study contributed equally to the treated (i.e., ultraviolet-irradiated) and control experiences. This was made possible by using two types of lamps and assigning them to the operating rooms at weekly intervals. If the lamps assigned to a particular operating room for a given week were ultraviolet lamps, the patients operated on in that room during that week were considered *treated* patients. If the lamps were those which produce similar light but no ultraviolet radiation, the patients were considered *control* patients. The lamp assignments were scheduled so that each operating room was irradiated for three weeks of each six-week period and so that the difference between the number of *treated* and the number of *control* operating rooms in use in a particular hospital during a given week was not greater than one.

The lamp randomization schedule was essentially unknown. The hospital engineer serviced the lamps once each week and exchanged ultraviolet and dummy lamps according to a schedule provided by the statistician. The treatment status (ultraviolet or no ultraviolet) of each patient in the study was not a part of his clinical records, but was determined later on the basis of the date and time of the operation and the operating room used. All clinical observations and bacteriologic studies were made and recorded in ignorance of treatment status.

Results of Air Sampling. The bacterial flora of the operating-room air was determined by exposing open Petri dishes to fallout for an hour each day. Plate locations were not specified, except that they had to be at normal operating-table elevation and had to remain the same for a given room. The plates were exposed to the air in pairs; one member of each pair was shielded in such a way that the surface of the nutrient agar was shaded from the ultraviolet radiation but not from vertical fallout. The shielding was proved effective when it was determined that the amount of radiation impinging on the surface of the shielded plates was too low to be detected by a sensitive direct-reading ultraviolet meter. Thus, once an organism fell to the nutrient surface of a shielded plate, its ability to form a colony was not impaired by continued radiation exposure.

Table 5. Effect of Shielding on Air-Sedimentation Plate Results - Control Rooms

Colonies/plate	Shielded		Unshielded	
	Number	Percent	Number	Percent
0 (sterile)	282	13.1	296	13.8
1 to 99	1,860	86.3	1,834	85.4
100 or more	13	0.6	18	0.8
Totals	2,155	100.0	2,148	100.0
Mean	15.69		16.00	

Table 6. Shielded Plate Colony Counts - Ultraviolet and Control Rooms

Colonies/plate	UV room		Control room	
	Number	Percent	Number	Percent
0 (sterile)	587	26.5	282	13.1
1 to 19	1,460	65.8	1,255	58.2
20 to 49	148	6.7	500	23.2
50 to 99	24	1.1	105	4.9
100 or more	0	0.0	13	0.6
Totals	2,219	100.1*	2,155	100.0

*Total other than 100.0 due to decimal rounding.

Although the shielding protected the sedimentation plate from radiation, it had no apparent effect on the fallout of organisms from the air. This was established by comparing shielded and unshielded plates exposed in the control rooms (Table 5). The similarity between the mean colony counts, 15.69/plate with and 16.00/plate without shielding, is striking and the difference, 0.31 colony/plate, is well within the limits of differences that chance could be expected to produce. There is no indication that the shields themselves carried organisms that added to the bacterial seeding of the shielded plates (note the similarity of the *100 or more* figures), or that the shielding obstructed the fallout of organisms from the air (note the similiarity of the *sterile* figures).

Table 7. Summary of Shielded Air-Sedimentation Plate Mean Colony Counts For Ultraviolet and Control Operating Rooms

Phase of study or operating room	Mean colony counts: UV room (2,219 plates summarized)	Mean colony counts: Control room (2,155 plates summarized)	Reduction in mean count with UV, percent
Entire study	6.85	15.69	56.3
low-intensity phase*	8.03	16.34	50.9
high-intensity phase*	5.54	14.97	63.0
Hospital 1**			
room 1	5.90	13.38	55.9
room 2	5.47	13.20	58.6
Hospital 2**			
room 2	5.04	13.58	62.9
room 3	4.55	9.63	52.8
room 4	4.08	11.36	64.1
Hospital 3**			
room 1	15.78	31.19	49.4
room 2	17.94	42.05	57.3
room 3	11.31	19.37	41.6
Hospital 4**			
room 1	1.74	4.21	58.7
room 2	6.09	14.79	58.8
room 3	5.77	14.62	60.5
Hospital 5***			
room 1	5.15	19.54	73.6 (high)
room 2	8.39	12.12	30.8 (low)
room 3	6.83	12.19	44.0
room 4	11.15	18.11	38.4
room 5	6.08	10.62	42.7

*See Chapter III ("Physical Factors...").

**Combined low- and high-intensity phases of study.

***High-intensity phase only.

The ability of ultraviolet radiation to reduce the number of viable organisms that settle from the air can be clearly demonstrated by comparing results obtained with shielded plates exposed in ultraviolet and control operating rooms (Table 6). Irradiation doubled the percentage of sterile plates (26.5% with and 13.1% without irradiation). Irradiation reduced by nearly three-fourths the proportion of plates with 20 or more colonies (7.8 *vs.* 28.7%), reduced by four-fifths the proportion of plates with 50 or more colonies (1.1 *vs.* 5.5%), and prevented colony counts of 100 or more.

The bactericidal effectiveness of ultraviolet radiation is further demonstrated by the average numbers of organisms recovered from the plates after one-hour exposure to fallout (Table 7). Over the entire period of study, the mean shielded-plate colony count for irradiated rooms was less than half the mean count for control rooms (6.85 *vs.* 15.69 colonies/plate, respectively). During the initial period, when the radiation was below protocol intensity, the mean colony count was reduced by 50.9 per cent; later, at protocol (increased) intensity, the mean count was reduced by 63.0 per cent.

The mean-count reduction associated with irradiation was observed for each of the 16 study operating rooms. The degree of reduction varied considerably, even within a given hospital, ranging from 30.8 per cent (Hospital 5, room 2) to 73.6 per cent (Hospital 5, room 1). Such factors as the size and shape of the room and the plate-exposure location within the room presumably influenced the percentage of airborne organisms killed.

Clinical Results. During the course of the study, a total of 15,613 operative wounds were observed, of which 1,157, or 7.4 per cent, were classified definitely

Table 8. Incidence of Infection, by Wound Classification and Treatment Status

Classification	Total wounds: UV	Total wounds: Control	Definite infections: UV: Number	Definite infections: UV: Percent	Definite infections: Control: Number	Definite infections: Control: Percent	Possible and definite infections: UV: Number	Possible and definite infections: UV: Percent	Possible and definite infections: Control: Number	Possible and definite infections: Control: Percent
Refined-clean	3,277	3,379	94	2.9	128	3.8	112	3.4	154	4.6
Other clean	2,458	2,576	180	7.3	192	7.5	215	8.7	226	8.8
Clean-contaminated	1,258	1,331	140	11.1	140	10.5	159	12.6	156	11.7
Contaminated	276	405	53	19.2	58	14.3	55	19.9	61	15.1
Dirty	288	293	89	30.9	77	26.3	89	30.9	82	28.0
Totals *	7,557	7,984	556	7.4	595	7.5	630	8.3	679	8.5

*Excluding 72 wounds of unknown classification.

Table 9. Incidence of Infection in Refined-Clean Wounds, by Hospital and Treatment Status

Hospital	Total wounds		Definite infections				Possible and definite infections			
			UV		Control		UV		Control	
	UV	Control	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Combined hospitals	3,277	3,379	94	2.9*	128	3.8	112	3.4**	154	4.6
Hospital 1	533	560	5	0.9	9	1.6	6	1.1	13	2.3
Hospital 2	804	807	27	3.4	43	5.3	27	3.4	44	5.5
Hospital 3	501	539	26	5.2	33	6.1	35	7.0	42	7.8
Hospital 4	429	464	3	0.7	4	0.9	3	0.7	4	0.9
Hospital 5	1,010	1,009	33	3.3	39	3.9	41	4.1	51	5.1

*Observed 0.9 fewer definite infections per 100 wounds; 95-percent confidence limits are 1.8 to 0.06 percent fewer infections (47.4 to 1.6 percent reductions).

**Observed 0.8 fewer possible plus definite infections per 100 wounds; 95-percent confidence limits are 2.1 to 0.2 percent fewer infections (45.7 to 4.3 percent reductions).

infected * by the physicians evaluating the wounds. The figures for each class of wound are set forth below and summarized in Table 8.

*Refined-Clean Wounds.*** If direct irradiation of the operating room influences the incidence of infection by minimizing airborne contamination, this benefit would be most apparent in refined-clean wounds, which are the least susceptible to contamination from sources other than the air. There were 6,656 refined-clean wounds followed during the study, of which 222 (3.3%) became definitely infected (Table 9). The incidence of infection in irradiated wounds was 2.9 per cent (94 infections in 3,227 wounds), and in control wounds was 3.8 per cent (128 infections in 3,379 wounds); the difference is significant at the 5 per cent level. The tendency for irradiated wounds to produce fewer infections than control wounds was evident in each of the five hospitals. Although no single hospital produced a sample large enough for the difference to be considered significant, the consistency observed among the five hospitals in the direction of irradiation effect itself would occur in only 3 per cent of repeated trials if irradiation were not reducing the incidence of wound infection.

The inclusion of those wounds which were considered possibly but not definitely infected after operation has little effect on the comparative results. The treated and control infection rates, with possible infections included in the infection category, were 3.4 and 4.6 per cent, respectively.

Other Clean Wounds. This classification comprises the clean wounds remaining when elective, primarily closed, undrained wounds are removed from the *clean* group. During the study, a total of 5,034 *other clean* wounds were followed, of which 372 (7.4%) developed infections. Wounds in this category thus had more than twice the incidence of infection observed for refined-clean wounds. There is no evidence that ultraviolet irradiation influenced the incidence of infection in this group (Table 10). The incidence of infection in treated wounds (7.3%) is only slightly lower than that in control wounds (7.5%). Furthermore, including possible infections has no effect on the comparison. There is no consistent treatment effect when the hospital experiences are examined separately.

* Throughout this report, all infection rates are *definite* infection rates unless otherwise specified, as in Tables 8 through 13.

** The five classes of wounds are defined in detail in Chapter III ("Wound Classification").

Table 10. Incidence of Infection in Other Clean Wounds, by Hospital and Treatment Status

Hospital	Total wounds		Definite infections				Possible and definite infections			
			UV		Control		UV		Control	
	UV	Control	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Combined hospitals	2,458	2,576	180	7.3*	192	7.5	215	8.7**	226	8.8
Hospital 1	361	379	13	3.6	22	5.8	16	4.4	23	6.1
Hospital 2	522	500	31	5.9	26	5.2	31	5.9	26	5.2
Hospital 3	405	478	41	10.0	65	13.6	59	14.6	86	18.0
Hospital 4	220	291	6	2.7	4	1.4	7	3.2	4	1.4
Hospital 5	950	928	89	9.4	75	8.1	102	10.7	87	9.4

*Observed 0.2 fewer definite infections per 100 wounds; 95-percent confidence limits are 1.6 percent fewer to 1.3 percent more infections (21.3 percent decrease to 17.3 percent increase).

**Observed 0.1 fewer possible plus definite infections per 100 wounds; 95-percent confidence limits are 1.6 percent fewer to 1.6 percent more infections (18.2 percent decrease to 18.2 percent increase).

Clean-Contaminated Wounds. The overall incidence of definite infection in clean-contaminated wounds was more than three times that in refined-clean wounds (10.8 *vs.* 3.3%). There is no evidence that irradiation of the operating rooms influenced the incidence of infection in this group (Table 11). The incidence of definite infection was slightly higher in irradiated wounds (11.1%) than in control wounds (10.5%), a tendency that persists when possible infections are included. Clean-contaminated wounds account for only 16.6 per cent of the total experience. Therefore, when the data are examined by hospital, the numbers of wounds in the irradiated and control categories are quite small and the variation that chance can produce in irradiated-*vs.*-control comparisons appears to be considerably in excess of whatever effect treatment has on the incidence of infection.

Contaminated Wounds. Postoperative wound infections were five times as frequent in contaminated wounds as in refined-clean wounds (16.3 *vs.* 3.3%), a

Table 11. Incidence of Infection in Clean-Contaminated Wounds, by Hospital and Treatment Status

Hospital	Total wounds		Definite infections				Possible and definite infections			
			UV		Control		UV		Control	
	UV	Control	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Combined hospitals	1,258	1,331	140	11.1*	140	10.5	159	12.6**	156	11.7
Hospital 1	230	198	16	7.0	25	12.6	18	7.8	27	13.6
Hospital 2	96	89	16	16.7	10	11.2	16	16.7	10	11.2
Hospital 3	223	225	49	22.0	39	17.3	64	28.7	51	22.7
Hospital 4	298	383	7	2.3	17	4.4	7	2.3	17	4.4
Hospital 5	411	436	52	12.7	49	11.2	54	13.1	51	11.7

*Observed 0.6 more definite infections per 100 wounds; 95-percent confidence limits are 1.8 percent fewer to 3.0 percent more infections (17.1 percent decrease to 28.6 percent increase).

**Observed 0.9 more possible plus definite infections per 100 wounds; 95-percent confidence limits are 1.6 percent fewer to 3.4 percent more infections (13.7 percent decrease to 29.1 percent increase).

Table 12. Incidence of Infection in Contaminated Wounds, by Hospital and Treatment Status

Hospital	Total wounds		Definite infections				Possible and definite infections			
			UV		Control		UV		Control	
	UV	Control	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Combined hospitals	276	405	53	19.2*	58	14.3	55	19.9**	61	15.1
Hospital 1	15	16	3	20.0	3	18.8	3	20.0	4	25.0
Hospital 2	30	23	10	33.3	6	26.1	10	33.3	6	26.1
Hospital 3	33	82	2	6.1	12	14.6	4	12.1	14	17.1
Hospital 4	85	164	7	8.2	6	3.7	7	8.2	6	3.7
Hospital 5	113	120	31	27.4	31	25.8	31	27.4	31	25.8

*Observed 4.9 more definite infections per 100 wounds; 95-percent confidence limits are 0.8 percent fewer to 10.5 percent more infections (5.6 percent decrease to 73.4 percent increase).

**Observed 4.8 more possible plus definite infections per 100 wounds; 95-percent confidence limits are 0.9 percent fewer to 10.6 percent more infections (6.0 percent decrease to 70.2 percent increase).

strong indication that contamination sources other than the operating-room air are largely responsible for the infections. When the incidence of infection in irradiated wounds is compared with that in control wounds (Table 12), there is no indication that ultraviolet irradiation has prevented any infections. In fact, the higher rate of infection in treated wounds (19.2 *vs.* 14.3%) suggests an increase in the risk of infection with treatment. The observed difference in infection rates is, however, still within the limits of that which chance alone might reasonably produce. Only one hospital (Hospital 3) produced a treated infection rate less than its control rate. Too few wounds were reported possibly infected (two treated and three control) to produce any change in the comparison when the definition of wound infection is relaxed.

Dirty Wounds. The very nature of this classification, old wounds of traumatic origin and wounds involving abscesses or perforated viscera, suggests frequent contamination of the operative field with potential pathogens and does not exclude the possibility of encountering an occasional frank infection in the field of operation. The incidence of infection in dirty

Table 13. Incidence of Infection in Dirty Wounds, by Hospital and Treatment Status

Hospital	Total wounds		Definite infections				Possible and definite infections			
			UV		Control		UV		Control	
	UV	Control	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Combined hospitals	288	293	89	30.9*	77	26.3	89	30.9**	82	28.0
Hospital 1	20	15	11	55.0	4	26.7	11	55.0	6	40.0
Hospital 2	53	38	23	43.4	17	44.7	23	43.4	17	44.7
Hospital 3	35	34	19	54.3	14	41.2	19	54.3	16	47.1
Hospital 4	100	130	11	11.0	13	10.0	11	11.0	13	10.0
Hospital 5	80	76	25	31.2	29	38.2	25	31.2	30	39.5

*Observed 4.6 more definite infections per 100 wounds; 95-percent confidence limits are 2.7 percent fewer to 12.0 percent more infections (10.3 percent decrease to 45.6 percent increase).

**Observed 2.9 more possible plus definite infections per 100 wounds; 95-percent confidence limits are 4.5 percent fewer to 10.3 percent more infections (16.1 percent decrease to 36.8 percent increase).

Table 14. Incidence of Infection in Refined-Clean Wounds, by Treatment Status, for Months of High and Low Risks of Infection

Season	UV wounds			Control wounds		
	Total	Definite infections		Total	Definite infections	
		Number	Percent		Number	Percent
Combined hospitals						
High-risk months	1,461	71	4.9	1,434	97	6.8
Low-risk months	1,816	23	1.3	1,945	31	1.6
Hospital 1						
High-risk months	212	5	2.4	233	9	3.9
Low-risk months	321	0	0.0	327	0	0.0
Hospital 2						
High-risk months	331	12	3.6	352	34	9.7
Low-risk months	473	15	3.2	455	9	2.0
Hospital 3						
High-risk months	274	22	8.0	247	25	10.1
Low-risk months	227	4	1.8	292	8	2.7
Hospital 4						
High-risk months	81	3	3.7	72	4	5.6
Low-risk months	348	0	0.0	392	0	0.0
Hospital 5						
High-risk months	563	29	5.2	530	25	4.7
Low-risk months	447	4	0.9	479	14	2.9

wounds (28.6%) is 8.7 times the rate for refined-clean wounds. The rate of definite infection (Table 13) in irradiated dirty wounds (30.9%) is somewhat higher than in the control wounds (26.3%). But the difference is no greater than that which would probably occur in one of four repeated trials with no ultraviolet irradiation. The comparison remains essentially the same when the five reported possible infections (all in control wounds) are included.

Risk of Infection and Irradiation Effect. It is reasonable to assume that the risk of airborne contamination in an operating room is not constant, but varies with seasonal changes in the prevalence of upper respiratory infections. Therefore, if ultraviolet irradiation reduces the incidence of postoperative infection in refined-clean wounds slightly during the entire course of the study, the beneficial effect of irradiation might be greater during periods of ordinarily high incidence of postoperative infection and smaller during periods of ordinarily low incidence. To investigate this possibility, the refined-clean wounds for each hospital were separated into:

1. Those occurring during months when the incidence of infection in both irradiated and control wounds was *above* the average for the particular hospital; and

2. Those occurring during months when the incidence of infection in both irradiated and control wounds was *below* the average for the particular hospital.

The results of this analysis are set forth in Table 14. When the risk of infection was *below* average, the combined-hospitals infection rate in irradiated wounds was 1.3 per cent and that in control wounds was 1.6 per cent. When the risk of infection was *above* average, the irradiated and control rates were 4.9 and 6.8 per cent, respectively. Although the absolute differences between infection rates were greater when the risk of infection was high than when it was low, the relative differences were about the same. The difference between these two estimates of irradiation effectiveness is within the limits of chance variation. The results are not consistent among the five hospitals, or even (in two cases) within a given hospital.

Intensity of Ultraviolet Irradiation. The observations discussed in the preceding sections are based on the entire experience of the study. When it was discovered that the ultraviolet-radiation intensities in the study operating rooms were generally below protocol requirements, the intensities were increased. The transitions from low to high intensity were not simultaneous in all institutions, however, but only as the changes in lamp installations in each hospital were completed. As a result, different hospitals did not contribute in the same proportion to the two phases of study. It was therefore necessary to adjust the observed infection rates to eliminate the effects of different intensities. The adjusted infection rates are shown in Table 15.

Table 15. Incidence of Infection, by Level of Ultraviolet Intensity, Wound Classification, and Treatment Status

UV intensity	Definite infections: UV wounds Number	UV wounds Percent	Control wounds Number	Control wounds Percent
All wounds**				
Low intensity	4,404	7.1	4,552	7.7
High intensity	3,190	7.5	3,467	7.0
Refined-clean wounds				
Low intensity	1,920	2.8	1,965	3.8
High intensity	1,357	2.9	1,414	3.6
Other clean wounds				
Low intensity	1,420	7.6	1,471	7.7
High intensity	1,033	7.0	1,105	7.0
Clean-contaminated wounds				
Low intensity	677	9.3	742	10.4
High intensity	581	13.0	589	10.7
Contaminated wounds				
Low intensity	163	16.3	179	16.3
High intensity	113	16.9	226	15.2
Dirty wounds				
Low intensity	196	27.0	175	31.8
High intensity	92	25.5	118	22.0

*Adjusted to distribution of wounds by hospital in combined low- and high-intensity phases.

**Includes 72 wounds of unreported classification.

Table 16. Incidence of Infection, by Level of Ultraviolet Intensity, Hospital, and Treatment Status

UV intensity	Definite infections: UV wounds Number	UV wounds Percent	Control wounds Number	Control wounds Percent
Combined hospitals				
Low intensity	4,404	7.2	4,552	8.0
High intensity	3,190	7.5	3,467	6.8
Hospital 1				
Low intensity	582	3.6	570	4.7
High intensity	581	4.8	605	6.0
Hospital 2				
Low intensity	950	7.2	904	8.3
High intensity	557	7.0	554	4.9
Hospital 3				
Low intensity	713	12.5	848	14.0
High intensity	492	9.8	520	8.8
Hospital 4				
Low intensity	667	3.1	701	3.4
High intensity	467	2.8	732	2.7
Hospital 5				
Low intensity	1,492	8.0	1,529	7.7
High intensity	1,093	10.2	1,056	10.0

During the low-intensity period of study, 2.8 per cent of the treated refined-clean wounds developed definite infections, compared with 3.8 per cent of the control wounds, a reduction with treatment of 1.0 infection/100 wounds, or 26 per cent of the control level. The reduction with high-intensity irradiation of the operating room was 0.7 infection/100 wounds, a relative decrease of 19 per cent. Although it might appear that high-intensity radiation was less effective than low-intensity radiation in preventing wound infections, there is no significant difference between the results at the two intensity levels. Examination of the effect of intensity in the remaining wound classifications and in the total experience reveals no significant differences in treatment effects. Furthermore, when the total experience is examined by

Table 17. Highest Rectal Temperature Recorded Postoperatively, by Treatment Status

Highest rectal temperature recorded	Total wounds		UV wounds		Control wounds	
	Number	Percent	Number	Percent	Number	Percent
Combined hospitals	15,291	99.9*	7,432	100.0	7,859	100.0
under 101 F	12,281	80.3	6,023	81.0	6,258	79.6
101 F or higher, but below 103 F	2,423	15.8	1,136	15.3	1,287	16.4
103 F or higher	587	3.8	273	3.7	314	4.0
Hospital 1	2,335	100.0	1,162	100.0	1,173	100.0
under 101 F	1,889	80.9	942	81.1	947	80.7
101 F or higher	446	19.1	220	18.9	226	19.3
Hospital 2	2,958	100.0	1,504	100.0	1,454	100.0
under 101 F	2,888	97.6	1,468	97.6	1,420	97.7
101 F or higher	70	2.4	36	2.4	34	2.3
Hospital 3	2,542	100.0	1,184	100.0	1,358	100.0
under 101 F	1,630	64.1	754	63.7	876	64.5
101 F or higher	912	35.9	430	36.3	482	35.5
Hospital 4	2,561	100.0	1,133	100.0	1,428	100.0
under 101 F	1,771	69.2	814	71.8	957	67.0
101 F or higher	790	30.8	319	28.2	471	33.0
Hospital 5	4,895	100.0	2,449	100.0	2,446	100.0
under 101 F	4,103	83.8	2,045	83.5	2,058	84.1
101 F or higher	792	16.2	404	16.5	388	15.9

*Total other than 100.0 percent due to decimal rounding.

hospital for each phase of study (Table 16), it can be seen that the observed effects of intensity are consistently greater for control wounds than for treated wounds, which makes it impossible to conclude that intensity had any effect on the influence of irradiation in preventing wound infection.

Febrile Response. Another measure of the effect of ultraviolet irradiation of the operating room on the patient's postoperative course is postoperative temperature. Although it has obvious limitations, this measure has two possible advantages over that of the incidence of wound infection: it is less susceptible to difference of opinion and the patient's temperature may be affected by wound infections too slight to be detected by direct observation. The patients' highest temperatures * were reported as, 1) below 101° F.; 2) 101° F. or higher, but below 103° F.; or 3) 103° F. or higher.

Of those recorded, rectal temperatures rose to 101° F. or higher for 19.7 per cent of the wounds (Table 17), 19.0 per cent for treated wounds and 20.4 per cent for control wounds. Temperatures of 103° F. or higher were recorded for 3.7 and 4.0 per cent of treated and control wounds, respectively. The data contained no evidence that the treatment effect differed by classification of operation, although the occurrence of fever differed between classifications, postoperative fever being least

* Oral temperatures were converted to rectal by adding 1° F.

Table 18. Summary of Tests of Significance of Observed Differences in the Incidence of Definite Postoperative Infections by Treatment Status for Subgroups Defined as to Specific Patient and Operative Characteristics (Minimum Comparison, 100 Treated and 100 Control Wounds)

Characteristic	Number of tests	Subgroups with significant treatment differences (5-percent level)	
		Favoring UV	Favoring absence of UV
Operative procedure	18	subtotal gastrectomy	operations on integument excluding excision of skin lesions with closure, primary skin graft, and burn graft
Diagnosis	14	benign neoplasm of uterus	--
Classification of wound* and:			
Hospital	20	--	--
Age	18	55-64 years (1)*	--
Sex	8	female (1)	male (4)*
Race	8	--	white (4)
Month and year of operation	27	--	October, 1961 (1)
Phase of study	8	--	high intensity (4)
Days of preoperative hospitalization	16	--	under 2 days (4)
Number of operative procedures	9	--	--
Closure type	4	primary (1)	--
Drain site provided	11	no (1)	--
Anesthesia	16	inhalation with intubation (1)	--
Patient factors predisposing to infection	6	no predisposing factors (1)	--
Time operation began	15	--	1230-1529 (4); 1530-2400 (4)
Duration of operation	17	2 hr-2 hr 59 min (2)	30-59 min (4)
Urgency	8	elective (1)	emergency (4)
Prophylactic antibiotics administered	7	--	--
Nature of final examination	14	--	--
Final clinical appraisal	4	--	--
Order of incision	5	--	first incisions (4)

*(1) Refined-clean; (2) other clean; (3) clean-contaminated; and (4) contaminated and dirty. Each significance test is an ultraviolet-*vs.*-control comparison within a subgroup of patients homogeneous as to both wound classification and the secondary characteristic named, e.g., patients aged 55 to 64 with refined-clean wounds.

likely to follow refined-clean wounds and most likely to follow dirty wounds.

Other Variables and Irradiation Effect. The search for ultraviolet effect was extended to possible links with other characteristics of patients and of operations within each classification of wound. Among the factors considered were the month and year of operation (Is ultraviolet benefit seasonal?), duration of operation (Is ultraviolet benefit more apparent following a longer operation with the attendant greater risk of contamination by airborne organisms?), type of operation, diagnosis, type of closure, and establishment of mechanical drain. However, because so many different operative procedures were used and so many diagnoses reported, to subdivide simultaneously by both operative procedure and wound classification, and by both diagnosis and wound classification, would have made the data fragmentary. Therefore, operative procedure and diagnosis were examined at the level of combined wound classifications. In all, the data were divided in 21 different ways (on the basis of 21 different variables) and 253 tests of significance were made of observed differences in the incidence of definite infection between ultraviolet and control wounds (Table 18). For each test, at least 100 ultraviolet and 100 control wounds identified as to infection were required.

Among the 72 tests on refined-clean wounds eight (11%—all but one favoring ultraviolet), and among the remaining 181 tests 13 (7%—three favoring ultraviolet and 10 adverse), were significant at the 5 per cent level. On no characteristic other than wound classification is there any accumulation of tests favoring ultraviolet irradiation. Beyond the wound classification itself, therefore, none of the factors thus studied seemed to identify a particular subset of patients for whom the advantage of ultraviolet irradiation was noteworthy.

Discussion: There can be no question concerning the ability of direct ultraviolet irradiation of operating rooms to reduce substantially the number of viable organisms recoverable from the air. During the entire period of study, ultraviolet irradia-

Table 19. Summary of Infections Following Operative Procedures Responsible for 100 or More Wounds

Operative procedure	All hospitals			Hospital 1			Hospital 2			Hospital 3			Hospital 4			Hospital 5		
	Number of wounds	Infections No.	Infections %	Number of wounds	Infections No.	Infections %	Number of wounds	Infections No.	Infections %	Number of wounds	Infections No.	Infections %	Number of wounds	Infections No.	Infections %	Number of wounds	Infections No.	Infections %
Excision lesion skin with closure	894	35	3.9	51	2	3.9	284	14	4.9	14	1	7.1	68	1	1.5	477	17	3.6
Excision lesion skin with graft	168	15	8.9	11	1	9.1	9	1	11.1	3	1	33.3	110	7	6.4	35	5	14.3
Partial mastectomy; excision lesion	827	18	2.2	236	4	1.7	153	4	2.6	66	4	6.1	38	0	0.0	334	6	1.8
Radical mastectomy	227	43	18.9	58	4	6.9	30	4	13.3	22	9	40.9	18	3	16.7	99	23	23.2
Excision bone lesion; biopsy bone; osteotomy	109	6	5.5	13	1	7.7	33	1	3.0	41	2	4.9	3	0	0.0	19	2	10.5
Open reduction: plate, screw, nail	144	6	4.2	12	0	0.0	64	2	3.1	53	3	5.7	1	0	0.0	14	1	7.1
Excision, intervertebral disc	212	3	1.4	92	1	1.1	3	0	0.0	7	0	0.0	0	0	-	110	2	1.8
Digit, amputation	126	21	16.7	2	0	0.0	34	8	23.5	9	2	22.2	63	5	7.9	18	6	33.3
Femur, amputation	101	18	17.8	3	0	0.0	9	3	33.3	15	4	26.7	33	1	3.0	41	10	24.4
Subtotal gastrectomy	288	29	10.1	30	3	10.0	50	4	8.0	27	6	22.2	80	0	0.0	101	16	15.8
Colostomy, exteriorization of cecum	140	27	19.3	9	1	11.1	14	7	50.0	34	5	14.7	42	2	4.8	41	12	29.3
Colectomy, partial, with anastomosis	220	22	10.0	38	4	10.5	15	3	20.0	40	8	20.0	38	2	5.3	89	5	5.6
Abdominoperineal resection	190	22	11.6	19	2	10.5	20	0	0.0	54	13	24.1	45	1	2.2	52	6	11.5
Appendectomy	551	63	11.4	17	6	35.3	46	6	13.0	90	12	13.3	226	6	2.7	172	33	19.2
Cholecystectomy, simple	756	52	6.9	107	1	0.9	104	8	7.7	63	5	7.9	117	6	5.1	365	32	8.8
Choledochostomy (with or without cholecystectomy)	111	19	17.1	20	2	10.0	20	2	10.0	22	8	36.4	8	0	0.0	41	7	17.1
Exploratory laparotomy (with or without biopsy)	321	25	7.8	18	2	11.1	38	1	2.6	99	13	13.1	103	2	1.9	63	7	11.1
Herniorrhaphy, inguinal, femoral, epigastric	1,312	25	1.9	247	2	0.8	215	2	0.9	105	4	3.8	302	4	1.3	443	13	2.9
Herniorrhaphy, incisional or ventral	314	12	3.8	24	1	4.2	57	3	5.3	23	1	4.3	130	2	1.5	80	5	6.2
Nephrectomy	127	22	17.3	8	2	25.0	21	3	14.3	44	8	18.2	1	0	0.0	53	9	17.0
Suprapubic or retropubic prostatectomy	167	19	11.4	40	4	10.0	24	3	12.5	34	9	26.5	2	0	0.0	67	3	4.5
Oophorectomy, uni-or bilateral	136	5	3.7	19	0	0.0	57	4	7.0	33	0	0.0	7	0	0.0	20	1	5.0
Hysterectomy (with or without salpingo-oophorectomy)	628	38	6.1	138	5	3.6	359	22	6.1	118	10	8.5	4	0	0.0	9	1	11.1
Exploratory thoracotomy (with or without biopsy)	137	8	5.8	61	3	4.9	6	0	0.0	12	1	8.3	15	0	0.0	43	4	9.3
Lobectomy, segmental resection	131	9	6.9	51	5	9.8	10	1	10.0	4	0	0.0	15	0	0.0	51	3	5.9
Mitral valvular procedure	120	5	4.2	11	0	0.0	0	0	-	5	0	0.0	8	0	0.0	96	5	5.2
Ligation veins, extremity	145	3	2.1	16	1	6.2	49	0	0.0	7	0	0.0	15	0	0.0	58	2	3.4
Stripping veins, extremity	204	12	5.9	69	0	0.0	1	0	0.0	30	3	10.0	38	0	0.0	66	9	13.6
Biopsy of lymph node	295	4	1.4	36	1	2.8	54	0	0.0	38	0	0.0	60	0	0.0	107	3	2.8
Thyroidectomy	406	9	2.2	97	0	0.0	51	0	0.0	28	2	7.1	44	0	0.0	186	7	3.8

tion reduced the number of recoverable viable organisms by 56.3 per cent (6.85 colonies/plate after a one-hour exposure in irradiated rooms *vs.* 15.69 colonies/plate in unirradiated rooms). Under the initial low ultraviolet intensity, the reduction in the mean number of colonies per plate was 50.9 per cent and under high-intensity irradiation, the reduction was 63.0 per cent.

Despite the reduction in viable airborne organisms, ultraviolet irradiation produced little, if any, reduction in the incidence of postoperative wound infection. Within 28 days of operation, 7.4 per cent of the irradiated wounds and 7.5 per cent of the control wounds became infected. A statistically significant reduction in postoperative wound infections occurred only in refined-clean wounds (from 3.8 to 2.9%). Only a slight difference favoring irradiation (from 7.4 to 7.3%) occurred in other clean wounds. Infections were encountered more frequently in irradiated wounds than in control wounds for the other three classes (11.1 *vs.* 10.5% in clean-contaminated, 19.2 *vs.* 14.3% in contaminated, and 30.9 *vs.* 26.3% in dirty wounds), but none of the differences was large enough to be statistically significant. When the three categories of nonclean wounds are combined, the incidence of infection in irradiated wounds is 15.5 per cent, and that in control wounds, 13.6 per cent. This difference might well be due to chance.

The incidence of infection in refined-clean wounds, during months when the combined (treated plus control) infection rates were above the hospital average, was 5.9 per cent (4.9% treated and 6.8% control). During the remaining months, the infection rate was 1.4 per cent (1.3% treated and 1.6% control). Ultraviolet irradiation was about equally effective in preventing postoperative infections during periods of high and low risk of infection. During the course of the study, 598 definite wound infections were observed in control wounds. Of these, 128 (21.4%) occurred in refined-clean wounds, the only category in which the infection rate was significantly altered by irradiation. On the basis of the observed infection rate in irradiated refined-clean wounds, it may be concluded that about 30 of the 128 infections could have been prevented by ultraviolet irradiation. The 95 per cent confidence interval on this estimate ranges from 2 to 61 fewer infections.

Type of Operation

One of the secondary benefits of this study has been the collection of unbiased data on the over-all incidence of infection in a large surgical experience. The incidence of infection has been determined for various specific operations and, in order to be meaningful, this compilation (Table 19) has been limited to operations that were responsible for 100 or more wounds during the course of the study. The compilation thus includes all pertinent operations performed, with and without ultraviolet irradiation.

Table 20 summarizes the incidence of infection among a small group of procedures that were performed frequently and presumably in a fairly standardized manner. The procedures are listed in order of increasing rates of infection. It is of interest that in this particular list, the operations with the lowest and the highest infection rates (herniorrhaphy and radical mastectomy, respectively) are both of the clean type, in which endogenous contamination should be minimal. However, the incidence of infection after radical mastectomy, a *clean* operation, was almost twice that of partial colectomy, a *clean-contaminated* procedure (18.9 and 10.0%, respectively). In most instances, these procedures were done for malignancy, and almost all were performed electively. Endogenous operative contamination must certainly have been inversely related to

Table 20. Incidence of Infection Following Selected, Commonly Performed Operative Procedures

Operative procedure	Number of times performed	Incidence of infection, percent
Herniorrhaphy*	1,312	1.9
Thyroidectomy	406	2.2
Hysterectomy	628	6.1
Cholecystectomy	756	6.9
Partial colectomy	220	10.0
Subtotal gastrectomy	288	10.1
Appendectomy	551	11.4
Nephrectomy	127	17.3
Radical mastectomy	227	18.9

*Including inguinal, femoral, and epigastric; excluding incisional and ventral.

the incidence of infection following the two procedures. The hazard of exogenous contamination should be approximately the same for each, which certainly suggests that radical mastectomy provided a more suitable medium for the growth of contaminating bacteria.

Although radical mastectomy resulted in an over-all incidence of infection of 18.9 per cent, excision biopsy of breast tissue resulted in an infection rate of only 2.2 per cent. The differences in duration of operation and magnitude of wound are obvious, but the individuals (possibly staphylococcus carriers) performing the operations were essentially the same. Similarly, choledochostomy (with or without cholecystectomy) resulted in an infection rate of 17.1 per cent, whereas cholecystectomy alone had an infection rate of only 6.9 per cent. These differences appear to be related to differences in duration and magnitude of the operation.

The infection rates after appendectomy (11.4%), subtotal gastrectomy (10.1%), and partial colectomy (10.0%) do not differ significantly.

Tables 9 through 13 illustrate the differences between hospitals in over-all incidence of infection. For example, after refined-clean operations, the incidence of definite infection ranged from 0.7 to 5.2 per cent with irradiation and from 0.9 to 6.1 per cent without irradiation. Similar variations are noted when infection rates for specific types of operations are compared. The infection rate after herniorrhaphy ranged from 0.8 to 3.8 per cent; after cholecystectomy, 0.9 to 8.8 per cent; after radical mastectomy, 6.9 to 40.9 per cent; etc. There was a general trend; a hospital having a high infection rate after one type of operation tended to have high rates after other types.

Analysis of the differences between hospitals is beyond the scope of this study; it may be stated here only that the differences cannot be explained on the basis of variations in patient selection or type of operation, of variations in the atmospheric bacterial flora of the various operating rooms, or of the incidence of staphylococcus carriers in the various units. As mentioned earlier, the study was designed to standardize reporting in an effort to make the data from various hospitals as comparable as possible.

Bacterial Contamination of Wound (as Indicated by Classification of Operation)

Of the many factors which influence the incidence of wound infection, bacterial contamination of the wound is perhaps the most obvious, having been accepted as a prerequisite for wound infection since Lister's time. Inasmuch as bacterial contamination is a "necessary, but not sufficient cause of wound infection," its role in the fate of a given wound may be obscured by other factors, e.g., when a grossly contaminated wound heals primarily.

It is recognized that operative contamination cannot be precisely measured by present bacteriologic technics, and that in some wounds (such as those which are drained or those not closed primarily) an

Table 21. Incidence of Infection, by Wound Classification and Hospital

Classification of operation	Number of wounds	Number of definite infections	Infection rates, percent					
			Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5	Combined
Refined-clean	6,656	222	1.3	4.3	5.7	0.8	3.6	3.3
Other clean	5,034	372	4.7	5.6	12.0	2.0	8.7	7.4
Clean-contaminated	2,589	280	9.6	14.1	19.6	3.5	11.9	10.8
Contaminated	681	111	19.4	30.2	12.2	5.2	26.6	16.3
Dirty	581	166	42.9	44.0	47.8	10.4	34.6	28.6
Not classified	72	6	9.1	0.0	11.1	0.0	8.1	8.3
Totals	15,613	1,157	4.8	7.0	11.7	3.0	8.8	7.4

unknown number of bacteria may gain access to the wound postoperatively. Despite these limitations, total bacterial contamination can be gauged roughly at the time of operation by the criteria incorporated into the definitions of the five classes of operation adopted for this study: refined-clean, other clean, clean-contaminated, contaminated, and dirty. In the study, each wound was classified on completion of the operative procedure. The criteria for each class follow:

Clean
- No inflammation
- No break in technic
- Neither gastro-intestinal nor respiratory tract entered, but transection of appendix or cystic duct considered clean in absence of acute inflammation
- Entrance of genito-urinary or biliary tract considered clean in absence of infected urine or bile
- Subdivided into *refined-clean* (elective, not drained, and primarily closed) and *other clean* (clean cases other than refined-clean)

Clean-contaminated
- Gastro-intestinal or respiratory tract entered without significant spillage
- Minor break in technic
- Entrance of genito-urinary or biliary tract in presence of infected urine or bile

Contaminated
- Major break in technic (e.g., emergency cardiac massage)
- Acute bacterial inflammation without pus
- Spillage from gastro-intestinal tract
- Traumatic wound, fresh, from relatively clean source

Dirty
- Presence of pus
- Perforated viscus
- Traumatic wound, old, or from dirty source

When infection rates are tabulated for each class of wound (Table 21), the rate of infection rises steadily from 3.3 per cent in the refined-clean group to 28.6 per cent in the dirty group. The differences among the groups are highly significant. When infection rates are tabulated by hospital a similar progression is noted (with one exception) in each hospital as bacterial contamination increases.

Table 22, derived from Table 21, shows the relative contributions of each class of wound to the total study and to the total number of infections. Refined-clean operations make up 42.6 per cent of the total operative experience, and all nonclean operations, only 24.7 per cent of the total. The refined-clean operations, however, produced fewer than 20 per cent of all the infections, and the nonclean, nearly half (48.1%).

Figure 10 shows the relationship of infection rate and classification of operation. The ordinate of this graph is infection rate, and the abscissa is number of wounds, expressed as a percentage of the total.

Table 22. Numbers of Wounds and Infections in Each Wound Classification

Class	Number of wounds	Fraction of total wounds, percent	Number of infections	Fraction of total infections, percent
Refined-clean	6,656	42.6	222	19.2
Other clean	5,034	32.2	372	32.2
All clean	11,690	74.8	594	51.4
Clean-contaminated	2,589	16.6	280	24.2
Contaminated and dirty	1,262	8.1	277	23.9
All nonclean	3,851	24.7	557	48.1
Unclassified	72	0.5	6	0.5
All wounds	15,613	100.0	1,157	100.0

Discussion: Classification of the operative procedure as described above is intended to yield a semiquantitative estimate of bacterial contamination of the wound at the time of operation. Bacterial contamination of the incision, thus estimated, is seen to be directly related to the incidence of wound infection.

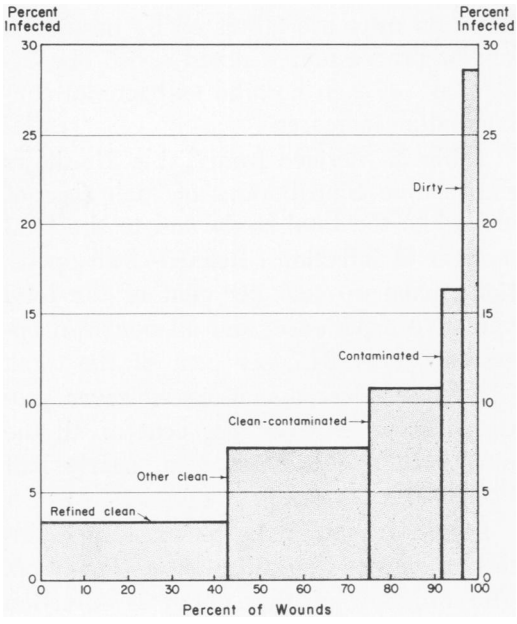

FIG. 10. Percentage of wounds infected, by classification of operation.

Although it has been demonstrated by many investigators (Hunt, 1933; Meleney, 1935; W. R. Culbertson *et al.*, 1961; Howe and Marston, 1962) that most, if not all, wounds are to some extent contaminated at operation, it would appear from our data that the *degree* of bacterial contamination is directly related to the risk of sepsis; i.e., a steady rise in infection rate is associated with increasing degrees of operative contamination, progressing from 3.3 per cent in refined-clean cases to 28.6 per cent in dirty cases.

The concept that the dosage or number of infecting organisms influences the risk of clinical infection is fundamental in laboratory investigation of infectious diseases and of clinical epidemiology. Moreover, several investigators studying surgical wound infections (Meleney, 1935; Murphy *et al.*, 1952; Jeffrey and Sklaroff, 1958), using classifications of the operative procedures similar to but not identical with those of the present study, have reported greater infection rates in the more contaminated procedures.

Emphasis will subsequently be placed on the role of local and systemic host defense factors, which may prevent the contaminating bacteria from establishing themselves and producing infection in the host tissues. That such host factors are very important can be ascertained from the data already presented: although 28.6 per cent of the dirty cases progressed to infection, the majority (71.4%) were considered to have healed without infection. Thus, for every operative wound there exists a complex interplay between the forces of bacterial invaders and the host's defenses. As a result of these multiple factors, a few *clean* wounds become infected and some massively *contaminated* wounds heal primarily.

Despite the importance of these nonbacterial factors in protecting the operative wound from infection, the data (Table 21, 22) strongly suggest the importance of the degree of bacterial contamination in determining wound infection rate. This striking association of increasing infection rate with increasing bacterial contamination cannot be explained on the basis of an increased incidence of poor-risk patients in the contaminated and dirty operative categories.

General Patient Factors

In the foregoing section, nonbacterial determinants of wound infection were alluded to—the host defense mechanisms that work to prevent bacterial contamination of most surgical incisions from causing clinical wound sepsis. This section deals with some general characteristics of the patient that may be related to such host defense mechanisms: age, race, sex, metabolism and nutrition (specifically, diabetes, steroid therapy, obesity, and malnutrition), and the presence of a clinical infection remote from the operative site. The observed relationships between these patient characteristics and wound infection rate are presented, with a consideration of these findings in the light of previously published clinical and experimental data.

Table 23. Incidence of Infection, by Age of Patient

Age, yr	Number of wounds	Number of infections	Infection rate, percent
< 1	271	14	5.2
1-14	1,062	51	4.8
15-24	1,245	59	4.7
25-34	1,767	98	5.5
35-44	2,619	155	5.9
45-54	3,039	229	7.5
55-64	2,774	261	9.4
65-74	2,014	216	10.7
75+	769	71	9.2
Unknown	53	3	5.7
Totals	15,613	1,157	7.4

Age. Wound infection rate is tabulated by age of patient for the entire study population in Table 23. Low rates are found in the youngest groups, with the lowest rate (4.7%) in the 15- to 24-year group. The infection rate steadily rises with age to the 65- to 74-year group, which has the highest rate, 10.7 per cent. A slight peak in the infection rate for the infant group and a slight drop for the oldest group are noted. Figure 11 shows this relationship between age and infection rate.

The same relationship is evident when the infection rates are analyzed for individual hospitals (Table 24), although the trend is not as regular as in the combined

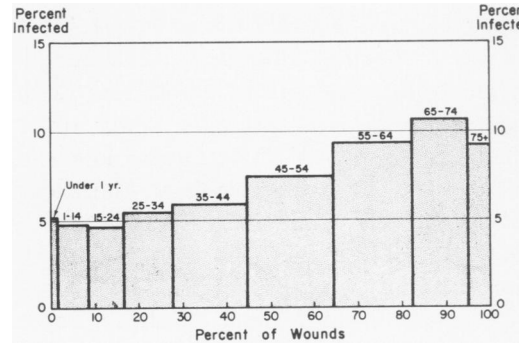

FIG. 11. Percentage of wounds infected, by age of patient.

Table 24. Incidence of Infection, by Age of Patient and Hospital

Age, yr	All hospitals			Hospital 1			Hospital 2		
	No. of wounds	Infections		No. of wounds	Infections		No. of wounds	Infections	
		No.	Percent		No.	Percent		No.	Percent
< 1	271	14	5.2	10	1	10.0	26	2	7.7
1-14	1,062	51	4.8	76	4	5.3	146	5	3.4
15-24	1,245	59	4.7	115	3	2.6	224	9	4.0
25-34	1,767	98	5.5	263	8	3.0	401	24	6.0
35-44	2,619	155	5.9	548	13	2.4	612	35	5.7
45-54	3,039	229	7.5	619	26	4.2	558	40	7.2
55-64	2,774	261	9.4	386	23	6.0	505	45	8.9
65-74	2,014	216	10.7	241	24	10.0	361	38	10.5
75+	769	71	9.7	68	9	13.2	125	11	8.8
Unknown	53	3	5.7	12	1	8.3	7	0	0.0
Totals	15,613	1,157	7.4	2,338	112	4.8	2,965	209	7.0

Age, yr	Hospital 3			Hospital 4			Hospital 5		
	No. of wounds	Infections		No. of wounds	Infections		No. of wounds	Infections	
		No.	Percent		No.	Percent		No.	Percent
< 1	68	6	8.8	94	0	0.0	73	5	6.8
1-14	273	22	8.1	336	6	1.8	231	14	6.1
15-24	313	27	8.6	239	4	1.7	354	16	4.5
25-34	320	21	6.6	302	5	1.7	481	40	8.3
35-44	364	50	13.7	316	9	2.8	779	48	6.2
45-54	375	47	12.5	350	19	5.4	1,137	97	8.5
55-64	406	58	14.3	374	15	4.0	1,103	120	10.9
65-74	325	53	16.3	327	12	3.7	760	89	11.7
75+	116	16	13.8	224	8	3.6	236	27	11.4
Unknown	13	2	15.4	5	0	0.0	16	0	0.0
Totals	2,573	302	11.7	2,567	78	3.0	5,170	456	8.8

hospital experience, presumably because of the small numbers of cases. The presence of the trend in every hospital lends credence to the belief that the observed direct variation of sepsis with age is fundamental.

The differences in infection rate with age might be due to some factor other than age itself. For example, nonclean wounds might preponderate in the older groups, which would increase their infection rates. Table B-1 * presents the infection rates in each age group for each class of wound. Table 25, derived from Table B-1, summarizes the infection rates by age for refined-clean and all clean wounds and compares them with the rates for all wounds. The same general trend of infection rate in clean wounds is evident, with the incidence of infection rising after the age of 14.

Examination of Table B-1 reveals, however, that different age groups contain different proportions of the various classes of wounds; for example, refined-clean wounds account for 58.0 per cent of the wounds in the 1- to 14-year group, and only 33.4 per cent of those in the 65- to 74-year group, and so on. However, such

* Tables whose designations are prefixed by "B" are grouped in Appendix B.

Table 25. Incidence of Infection, by Age of Patient and Wound Classification

Age, years	Refined-clean		All clean		All wounds	
	Number of wounds	Infection rate, percent	Number of wounds	Infection rate, percent	Number of wounds	Infection rate, percent
< 1	169	3.6	234	3.4	271	5.2
1-14	616	2.3	859	3.3	1,062	4.8
15-44	2,596	2.9	4,420	4.1	5,631	5.5
45-54	1,276	3.1	2,339	4.9	3,039	7.5
55-64	1,054	4.5	1,972	6.5	2,774	9.4
65-74	673	4.0	1,331	7.2	2,014	10.7
75+	246	5.3	487	7.2	769	9.2
Unknown	26	0	48	2.1	53	5.7
Totals	6,656	3.3	11,690	5.1	15,613	7.4

differences can be statistically corrected by the direct method of adjustment (explained below). When the infection rates are adjusted to overcome this bias, the incidence of wound infection is still found to increase with age (Table 26).

Adjusted Wound Infection Rates. A comparison of wound infection rates for two or more groups of patients will be influenced by all differences between the groups, not only by the primary difference used to define the groups. Thus, when we divide our study experience into age groups, the resulting comparisons of infection rates would be influenced not only by age, but also by other factors associated with age. One such factor is the class of operation; 58.0 per cent of the wounds in the 1- to 14-year group were refined-clean, but only 33.4 per cent of those in the 65- to 74-year group.

One method of coping with this situation is to compare age-specific infection rates within each wound classification (as in Tables 25 and B-1). However, this method requires that five separate comparisons be made, one for each wound classification, and produces no summary infection rates for descriptive use.

It is possible to combine the five separate rates for each age group into a single standardized rate. The use of such rates removes from the age comparison the effect of differences among the age groups in wound classification. In this study, the direct method of standardization or adjust-

Table 26. Incidence of Infection, by Age of Patient, Unadjusted and Adjusted for Selected Factors

Age, years	Unadjusted rate, percent	Infection rates, percent, adjusted for								
		Classification of wound	Duration of operation	Hospital	Preoperative hospitalization	Urgency of operation	Diabetes	Steroid therapy	Obesity	Malnutrition
< 1	5.2	6.6	4.5	6.7	5.6	5.3	*	*	*	*
1-14	4.8	5.4	5.5	5.1	5.3	4.4	*	*	*	*
15-24	4.7	4.6	4.7	4.3	5.4	4.3	*	4.7	4.7	*
25-34	5.5	5.6	5.7	5.7	5.9	5.5	*	5.4	5.5	*
35-44	5.9	6.4	6.1	6.2	6.1	6.1	5.8	5.8	5.8	*
45-54	7.5	8.0	7.5	7.8	7.5	8.1	7.5	7.6	7.6	7.5
55-64	9.4	9.0	9.0	9.2	9.0	9.3	9.4	9.3	9.4	9.4
65-74	10.7	9.7	10.3	10.7	9.9	10.9	10.7	10.8	10.7	10.7
75+	9.2	8.4	9.0	10.3	9.0	8.7	9.1	*	*	*
Total	7.4									

*Fewer than 10 patients with specific metabolic or nutritional conditions; adjusted rates not computed.

Table 27. Incidence of Infection, by Sex of Patient

Sex	Number of wounds	Number of infections	Infection rate, percent
Male	7,356	588	8.0
Female	8,242	568	6.9
Unknown	15	1	6.7
Totals	15,613	1,157	7.4

ment is used.** Thus, to remove from the age comparisons the effect of associated variation in wound classification, a standard population is first defined with respect to the variable requiring adjustment, in this illustration the wound classification. A convenient choice for the standard is that of the entire sample of 15,613 wounds (Table 8). Next, the observed rate for each age—wound-classification group is multiplied by the standard population weight for that wound classification to determine the number of infections expected in the standard population for that wound classification. All the expected infections for any age group are then summed over the wound classes and this sum is divided by the standard population total to yield the adjusted rate for that age group. Because the same standard population (i.e., with the same distribution of refined-clean, other clean, clean-contaminated, contaminated, and dirty procedures in each age group) is used in adjusting the infection rate for each age group, the effect of differences due to operative contamination as measured by classification of operation is eliminated.

Where specified throughout this chapter, infection rates have been adjusted to facilitate comparisons other than of age-specific infection rates and to remove differences other than those due to classification of operation. In each instance, the method employed is similar to that described above.

As will be demonstrated later, the incidence of infection is markedly influenced by such other factors as the hospital in which the operation was performed, the duration of the operation, nutritional and metabolic factors of the patient, and the duration of the patient's preoperative hospitalization. From data presented in Tables B-2 through B-5, the infection rates in each age group can be adjusted for all these factors (Table 26). It is observed that for the adjusted rates, the same general trend persists—after infancy and childhood, increasing age is associated with an increasing incidence of wound infection.

Discussion: The lowest unadjusted infection rate noted, 4.7 per cent, was found in the 15- to 24-year group. After age 24, the infection rate rises steadily with age to the 65- to 74-year group, in which the infection rate is 10.7 per cent. This increase in the infection rate with age cannot be explained on the basis of the other factors surveyed.

Increasing susceptibility to infection in older persons has been recognized clinically by many surgeons. Elman (1952) stated, "the resistance of the older individual to various infections is in general much lower than it is in the younger individual." Higher rates of wound sepsis in older patients have been noted by the Public Health Laboratory Service in a study of surgical infection in England and Wales (1960) and by Barnes and coworkers (1961, 1962) in a retrospective analysis of wound infections following herniorrhaphies, hysterectomies, appendectomies, and gastrectomies. In a statistical analysis of the British study, Lidwell (1961) concluded that age influences infection rate independently of duration of operation and other factors.

** Vital Statistics Rates in the United States: 1900–1940, Chapter 4. Adjusted Death Rates and Other Indices of Mortality. Washington, D. C.: United States Government Printing Office, 1943.

Table 28. Incidence of Infection, by Sex of Patient and Hospital

Sex	Infection rates, percent					
	Combined hospitals	Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5
Male	8.0	5.3	8.5	12.0	3.2	9.6
Female	6.9	4.4	6.1	11.5	2.9	8.1
Totals	7.4	4.8	7.0	11.7	3.0	8.8

One may speculate that specific cellular or humoral mechanisms of host resistance to infection and host wound healing, optimum in the young, gradually decline in efficiency after age 25. Baumgartner (1934) presented evidence that old age is a period of poor antibody production, and Du Noüy (1916) and MacNider (1952) demonstrated the detrimental effect of aging on repair of various tissues. There is also evidence that the host's defense mechanisms, both cellular and humoral, are less effective in the very young than at maturity. Matoth (1952) demonstrated that phagocytic ability and ameboid movement of leukocytes of newborn infants are inferior to that of leukocytes of adults, and J. T. Culbertson (1939) showed that the macrophages of suckling animals are less phagocytic than those of adults. The early deficiency in antibody production in infants, documented by Osborn *et al.* (1952), is well known to pediatricians. Such observations may explain in part the high infant infection rates found in this study.

It is concluded that the age of the patient probably plays a significant and direct role in determining the risk of surgical wound infection. Except at the extremes of life, increasing age is associated with an increasing infection rate.

Sex. Infection rates are divided by sex in Table 27, which shows the rate in males to be 8.0 per cent, and that in females, 6.9 per cent. The rate was higher in males for each of the five hospitals (Table 28).

A greater number of nonclean wounds occurring in males may account for the higher infection rate in males. Table B-6 partially substantiates that hypothesis. Clean wounds accounted for 79.6 per cent of the wounds in females and only 69.6 per cent of those in males. Moreover, the clean-wound infection rate is slightly lower in males than in females (4.9 and 5.2%, respectively). The nonclean-wound infection rate, however, is higher in males than females (15.1 and 13.6%). When the direct method of adjustment is used to correct for differences in wound classification, the adjusted infection rate in males becomes very similar to that in females (7.6 and 7.3%, respectively). Table 29 and Figure 12 summarize these rates.

Discussion: A slightly higher infection rate in males than in females was observed by the Public Health Laboratory

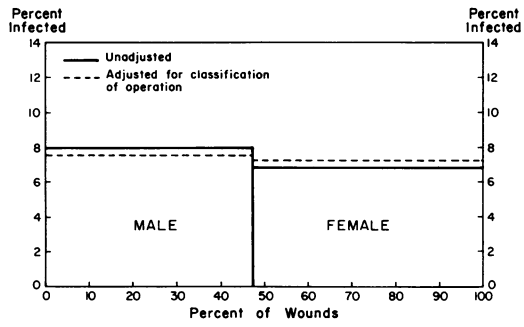

FIG. 12. Percentage of wounds infected, by sex of patient.

Table 29. Incidence of Infection, by Sex of Patient, Unadjusted and Adjusted for Wound Classification

Sex	Unadjusted infection rates, percent			Infection rates for wounds adjusted for class of wound, percent
	Clean wounds	Nonclean wounds	All wounds	
Male	4.9	15.1	8.0	7.6
Female	5.2	13.6	6.9	7.3
Totals	5.1	14.5	7.4	

Service (1960), in surveying surgical wound infections in England and Wales, where 10.3 per cent of males and 9.3 per cent of females were found to have septic wounds.

In our study, the increased incidence of wound infection in males is largely explained by the performance of more contaminated procedures on males. Using the direct method of adjustment to correct infection rates for wound classification, the infection rates in males and females become essentially the same. Thus, it appears that the sex of the patient is not a primary determinant of the risk of wound sepsis.

Race. Table 30 summarizes the relationship of race to infection rate. In the total population, the infection rate is higher, but not significantly so, in white patients (7.6%) than in nonwhite patients (6.8%). This rather unexpected finding can be explained on the basis of the individual hospital rates. Only Hospitals 3 and 4 had higher infection rates in whites than in nonwhites, and only Hospital 5 had a statistically significant difference between the white and nonwhite rates, with the white rate (8.0%), lower than the nonwhite rate (13.3%). The five hospitals show no consistent pattern. The lower combined-hospital infection rate for nonwhites results from the concentration of nonwhite patients (41.5%) in the experience of Hospital 4, which had the lowest over-all infection rate (3.0%), the lowest white rate (3.4%), and the lowest nonwhite rate (2.7%). The difference between the white and nonwhite rates at Hospital 4 is not statistically significant. This difference in hospital contribution to each racial group can be adjusted for as previously described. Race-specific infection rates, adjusted for hospital composition, are calculated (Table B-7), and summarized in Table 31. When adjusted, a higher infection rate in nonwhites (8.6%) is evident and a lower rate for whites (7.1%). The relationship of race to infection rate and the effect of adjustment for hospital are shown in Figure 13.

Other factors that might influence race-specific infection rates are the metabolic and nutritional status of the patient, age, and wound classification, all of which might

Table 30. Incidence of Infection, by Race of Patient and Hospital

	White			Nonwhite		
	Number of wounds	Number of infections	Infection rate, percent	Number of wounds	Number of infections	Infection rate, percent
Hospital 1	1,892	83	4.4	430	29	6.7
Hospital 2	2,184	147	6.7	768	62	8.1
Hospital 3	2,265	275	12.1	135	10	7.4
Hospital 4	1,057	36	3.4	1,500	41	2.7
Hospital 5	4,347	348	8.0	780	104	13.3
Totals	11,745	889	7.6	3,613	246	6.8

Table 31. Incidence of Infection, by Race of Patient, Unadjusted and Adjusted for Selected Factors

Race	Unadjusted infection rates, percent	Infection rates, percent, adjusted for						
		Hospital	Classification of wound	Age	Diabetes	Steroid therapy	Obesity	Malnutrition
White	7.6	7.1	7.8	7.5	7.6	7.6	7.5	7.6
Nonwhite	6.8	8.6	6.3	7.2	6.7	6.7	6.7	6.7
Total	7.4							

affect one race more than the other. When these differences are adjusted (Tables B-8–B-10), it is noted that the adjustments change the crude rates only slightly (Table 13).

Discussion: Apparent racial differences in susceptibilty to many infectious diseases, such as tuberculosis, yellow fever, influenza, and erysipelas, have been described (Rich, 1951; Burrows, 1959). Differences in attack rate, of course, cannot be construed as evidence of varying host resistance unless many other factors, such as incidence of exposure and general patient condition, are controlled. In this study, the unadjusted wound infection rate is insignificantly higher in whites than in nonwhites; this finding appears due to the unique infection rates and racial composition of the Hospital 4 experience. When statistical adjustment is made to correct for variation in hospital composition, infection rates of 7.1 and 8.6 per cent are obtained for whites and nonwhites, respectively. The adjusted rates probably represent the relative risk of infection between white and nonwhite more realistically than the crude rates.

Even if the hospital-adjusted race-specific rates are accepted, the difference apparently related to race is so small in comparison with many of the other factors that influence infection rate (e.g., wound classification, age, duration of surgery, etc.), that race cannot be considered a major factor in the determination of infection rate under the conditions of this study.

Metabolism and Nutrition. Clinical experience has indicated that certain nutritional and metabolic factors affect a patient's general resistance to infection. Four specific factors relating to the metabolic or nutritional status of the patient were reported in this study: 1) diabetes; 2) steroid therapy; 3) severe obesity; and 4) severe malnutrition. The incidences of infection in the patients manifesting these states are shown in Table 32.

The infection rate for each of these four special groups is significantly higher than the 7.1 per cent in those patients who had none of these nutritional and metabolic conditions. The relationship of these factors to wound infection rate is shown in Figure 14.

As is the case with other factors, such as sex and race, the high infection rates

Table 32. Incidence of Infection, by Presence of Certain Metabolic and Nutritional Conditions

Factors	Number of wounds	Number of infections	Infection rate, percent
None	14,800	1,046	7.1
Diabetes	356	37	10.4
Steroid therapy	119	19	16.0
Severe obesity	166	30	18.1
Severe malnutrition	67	15	22.4
Unknown	129	12	9.3
Totals*	15,613	1,157	7.4

*A few patients had more than one of the specific factors listed, so the sums of the wounds and infections exceed the totals.

Table 33. Incidence of Infection, by Presence of Certain Metabolic and Nutritional Conditions, Unadjusted and Adjusted for Selected Factors

Metabolic or nutritional factor	Unadjusted infection rates, percent	Infection rates, percent, adjusted for					
		Classification of wound	Hospital	Age	Duration of operation	Urgency of operation	Duration of preoperative stay
Diabetes	10.4	7.9	11.8	7.2	10.5	9.9	9.1
Steroid therapy	16.0	15.2	12.7	12.2	10.2	14.0	13.2
Obesity	18.1	17.2	18.2	18.5	16.5	18.0	18.3
Malnutrition	22.4	13.7	9.3	18.9	16.2	21.0	27.4
No metabolic or nutritional factor	7.1						
Total group	7.4						

found in association with these factors may be due to a related high incidence of contaminated procedures, long procedures, or aged patients. To correct for such a possible bias, the direct method of adjustment is used to eliminate differences due to age, wound classification, duration and urgency of operation, duration of preoperative hospitalization, and hospital composition (Tables B-4, B-11–B-14, and B-45). These adjusted rates are listed in Table 33. The possible influence of each of these factors on the relation of metabolism and nutrition to infection rate is outlined below.

Table B-11 presents the infection rates for patients with diabetes, receiving steroids, etc., according to the classification of operation. Although only about 25 per cent of the total study operations involved nonclean procedures—clean-contaminated, contaminated, and dirty (Table 22)—nonclean procedures were associated with 39.3 per cent of the operations on diabetics and 67.2 per cent of the operations on severely malnourished patients. Correction for these high proportions by the direct method of adjustment yields infection rates adjusted for classification of operation (Table 33). This adjustment lowers the infection rates for diabetics and the severely malnourished considerably, but lowers the rates for pa-

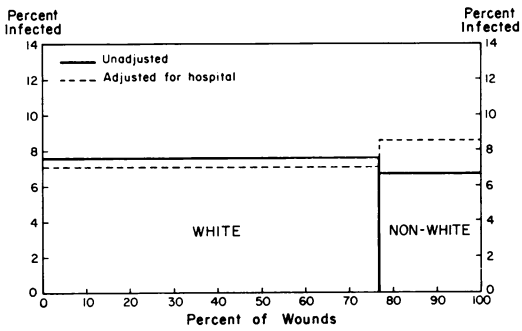

FIG. 13. Percentage of wounds infected, by race of patient.

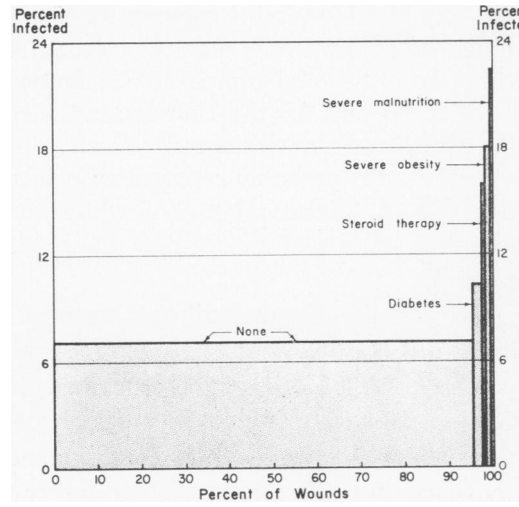

FIG. 14. Percentage of wounds infected in relation to metabolic and nutritional complications.

tients receiving steroid therapy and severely obese patients only slightly.

Table B-45 presents the crude infection rates for patients with diabetes, receiving steroids, etc., for each of the five study hospitals, with infection rates for these specific metabolic and nutritional factors adjusted for hospital distribution. These adjusted rates are summarized in Table 33. Correction for hospital distribution does not greatly influence the infection rates of diabetics or obese patients, but considerably lowers the rates for patients receiving steroids and for the malnourished. The size of the reduction for the latter group is obviously associated with over half of all the malnourished patients' being operated on at Hospital 3, the hospital with the highest infection rate. The adjusted infection rate, 9.3 per cent, reflects the theoretical risk of infection in the malnourished patients in this study if they were distributed uniformly among the five hospitals.

Calculations based on Table B-4 show that, although only 35.6 per cent of the total study population was 55 years old or over, 71.6 per cent of the diabetics, 50.4 per cent of those receiving steroid therapy, 42.2 per cent of the extremely obese, and 64.2 per cent of the severely malnourished were 55 or over. If age itself is a determinant of infection rate, the high concentrations of older patients in those groups manifesting the specific metabolic and nutritional factors must be corrected for (Table 33). Correction for age reduces the diabetic infection rate from 10.4 to 7.2 per cent. Similar age adjustments of the rates for the other three factors yield lower, but still relatively high, rates, except for the obese, whose rate is increased slightly.

From Table B-12, it can be calculated that operations performed on patients with specific metabolic and nutritional conditions tended to take longer than operations on other patients, and took longest in the obese and steroid-treated. Of the last two groups of patients, 7 to 12 per cent of the operations lasted over 5 hours, but only 3.9 per cent of all the operations in the study lasted over 5 hours. Because, as will be demonstrated later, duration of operation affects infection rate independently, rates adjusted for duration of operation are calculated from Table B-12 and summarized in Table 33. Adjustment for duration of surgery lowers the infection rate of steroid-treated and malnourished patients considerably and the rate for the severely obese slightly, and hardly changes the rate for diabetics.

It will be demonstrated later that the infection rate is higher after urgent or emergency operations than after elective operations. Table B-13 cross-tabulates the incidence of infection by the nutritional and metabolic status of the patient and by urgency of operation. The percentage of urgent and emergency operations among diabetic, steroid-treated, very obese, and malnourished patients is slightly higher (15.7 to 28.4%) than the percentage among the total study population (14.0%). The infection rates for these specific patient conditions adjusted for urgency of operation are only slightly lower than the unadjusted rates, indicating that urgency of operation and patient metabolism and nutrition act generally independently in influencing infection rate.

Patients whose preoperative hospital stays were prolonged had infection rates higher than the rate for the entire sample studied (see below, under *Preoperative and Postoperative Factors*). Without determining whether prolonged preoperative hospitalization is itself a primary determinant of wound infection, the association between the specific metabolic and nutritional factors under consideration and the duration of preoperative hospitalization was investigated (Table B-14). The median preoperative stay for diabetics was 6.1 days, for patients on steroids, 10.0 days, for severely obese patients, 3.7 days, and for severely malnourished patients, 8.9

days, compared with the median preoperative hospitalization for patients with no metabolic or nutritional factor, 2.2 days. Because of the prolonged preoperative stays of the patients with metabolic and nutritional problems, their infection rates, adjusted for duration of stay, were calculated (Table 33). Adjustment for duration of preoperative stay does not alter the infection rates for the severely obese, causes a slight to moderate reduction in the rates of diabetics and patients on steroid therapy, and actually increases the infection rate in the severely malnourished.

Discussion. The infection rates for each of the specific metabolic and nutritional factors investigated were considerably higher than the infection rate for the total study population. Although these groups combined represent less than 5 per cent of all the patients in the study, the difference between the infection rate for each group and the rate for the remainder of the sample is statistically significant. Thus, the specific conditions, although infrequent, must be regarded as associated with high rates of infection.

Diabetes. The assumption that diabetics are more susceptible to infection than nondiabetics has been generally accepted by physicians and surgeons alike (Forsham, 1960; Dineen, 1961). Animal experiments have indicated that wound healing is impaired in uncontrolled diabetes (Rosen and Enquist, 1960; Rosenthal *et al.*, 1962), that diabetic acidosis delays the early granulocytic phase of local cellular response to inflammation (Perillie *et al.*, 1961), and that acidosis is detrimental to host resistance to septicemia (Grogan and Artz, 1962).

However, Robbins and Tucker (1944) have presented autopsy evidence indicating that the incidence of many infections is essentially the same for diabetics and nondiabetics. Two important exceptions, pyelonephritis and infections of the extremities, occurred more frequently among diabetics, which the authors attributed to the increased frequency of bladder catheterization and more prevalent peripheral vascular disease in diabetics.

The subject of infection and diabetes has been concisely summarized by Schneierson (1962), who concluded that the diabetic patient in ketosis, rather than the well-controlled diabetic, is unusually susceptible to infection.

In this study, the incidence of surgical wound infection in 356 diabetic patients was 10.4 per cent, significantly higher than the over-all infection rate, 7.4 per cent. It would appear, however, that the higher rate of infection in diabetics is explained entirely on the basis of the large number of elderly patients constituting the diabetic group, for the age-adjusted rate of diabetics is the same as the rate of the nondiabetic group. Diabetes may be but one of many senescent changes which impair the elderly patient's resistance to infection. Inasmuch as infection rates rise with age after 14 years, even without diabetes (Table B-4), the general process of aging appears to be responsible for the increased infection rate in diabetics, rather than the large group of infection-prone diabetics' being responsible for increased infection rates in the elderly.

Steroid Therapy. Although adrenocorticosteroids have been used to treat some infectious diseases, it is generally believed that the symptomatic relief observed must be weighed against the potential danger of suppressing the host's response to the infection. In animal experiments, both ACTH and cortisone have been shown to increase susceptibility to a wide variety of bacterial agents, including such common wound pathogens as *Staphylococcus aureus* (Kligman *et al.*, 1951) and coliform organisms (Berlin *et al.*, 1952). The mechanisms involved in this weakening of host defenses may include 1) depression of antibody formation (Germuth *et al.*, 1951); 2) altered vascular reactivity to

local irritants (Ebert and Wissler, 1950, 1951); 3) diminished phagocytic capacity of polymorphonuclear leukocytes (Crepea *et al.*, 1951); and 4) suppression of the reparative process of new capillary formation and fibrogenesis (Howes *et al.*, 1950; Ragan *et al.*, 1950). The experimental and clinical evidence and the implications of this deleterious effect of adrenocorticosteroids on host resistance have been summarized by Kass and Finland (1953) and Thomas (1955).

In this study, the infection rate for the 119 patients receiving steroid therapy was 16.0 per cent, more than twice the rate for all patients. However, patients receiving steroid therapy tended to be older, had longer procedures, and stayed in the hospital longer preoperatively than the average patient. Each of these associated factors contributed somewhat to a higher infection rate, although the susceptibility of steroid-treated experimental animals to infection lends credence to the possibility that steroid therapy itself lowers resistance to infection.

Obesity. The poor tolerance of fatty tissue to bacterial contamination has long been noted clinically. Recent studies by Alexander *et al.* (1962–1963) have demonstrated that both blood volume and blood flow per unit weight are lower in adipose tissue than in lean tissue. This relative avascularity of adipose tissue may explain the apparent susceptibility of fat to infection and, perhaps, the high incidence of wound infection in the obese patient.

In the present study, severe obesity was associated with an infection rate of 18.1 per cent and, although operative procedures on these patients tended to be longer than the average, adjustment for duration of operation reduced the rate only slightly, to 16.5 per cent. No other factor was observed to be associated with obesity or responsible for the high infection rate manifested by these patients. Although severe obesity was encountered in only 166 of the 15,613 wounds studied, the infection rate in this small group was so high that it seems reasonable to ascribe most of it to the impaired resistance of the fatty tissues incised.

Table 34. Incidence of Infection, by Presence of Remote Infection

Presence of remote infection	Number of wounds	Number of infections	Infection rate, percent
No	14,732	993	6.7
Yes	799	147	18.4
Unknown	82	17	20.7
Totals	15,613	1,157	7.4

Malnutrition. The degree to which malnutrition predisposes to surgical wound infection is an unsettled issue. Cannon (1943, 1944, 1945), in discussing the importance of proteins in host resistance to both medical and surgical infections, emphasized that protein depletion may be associated with poor antibody response. There is also some evidence to indicate that in experimental animals the phagocytic activity of leukocytes is impaired by vitamin and protein deficiencies (Cottingham, 1943; Mills, 1943). On the other hand, Balch, finding excellent antibody responses in cachectic patients and normal phagocytic activity of granulocytes in a similar group (1954), questioned the importance of malnutrition in the genesis of surgical wound infection (1958).

Of the 67 severely malnourished patients who underwent surgery in this study, 15 developed wound infection (22.4%), suggesting that this group of patients represents a population of extremely high risk. These patients, however, tended to be older, had longer operations, and were more likely to have contaminated operations than the average. Moreover, 35 of the 67 underwent surgery at Hospital 3, where the infection rate for all patients was 11.7 per cent. Of the associated factors, hospital distribution and wound classification were by far the most important in influencing the infection rate in the malnourished patients. Adjustment for hospital distribution

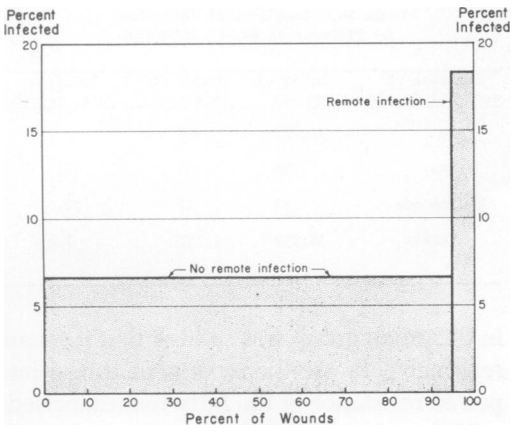

FIG. 15. Percentage of wounds infected in relation to remote infection.

lowers the infection rate for the malnourished from 22.4 to 9.3 per cent, and adjustment for wound classification lowers the rate to 13.7 per cent. The combination of irregular hospital distribution and the greater frequency of contaminated wounds may be responsible for the extremely high infection rate found in the malnourished patients. But it is also possible that malnutrition itself detrimentally affects resistance to infection in the same way that isolated depletion states in experimental animals affect wound healing, antibody formation, and phagocytosis.

Remote Infection. Infections other than in the area of the operative incision (referred to hereafter as remote infection) were recorded if they were present during the prescribed period of observation (28 days after operation or until wound infection was noted if that was before the 28th postoperative day). The infection rates in patients with and without remote infections are presented in Table 34.

The wound infection rate in patients with other septic conditions was 18.4 per cent, in contrast to a rate of 6.7 per cent in those without remote infection. Remote infections occurred in the genito-urinary, respiratory, and gastro-intestinal tracts, the skin, and the blood; genito-urinary and respiratory infections were most frequent. All types of remote infection were associated with a strikingly high wound infection rate. The relationship between the presence of remote infections and wound infection is shown in Figure 15.

The direct method of adjustment was used to correct for possible differences in the composition of the two groups (those with and without remote infection), adjusting for each of the other patient and operative factors known to exert a major influence on wound infection rate (Tables B-15–B-20 and B-46). The adjusted rates, summarized in Table 35, do not differ substantially from the crude rates, indicating that the presence of remote infection influences wound infection rate independently. Conversely, adjustment for remote infection of the rates for the other specific factors (Table 36) does not produce substantial changes, which is further evidence that the presence of remote infection acts independently in influencing wound infection rate.

Discussion: A striking increase in the wound infection rate has been noted in patients with remote infection, and is not explained by any other characteristic of

Table 35. Incidence of Infection, by Presence of Remote Infection, Unadjusted and Adjusted for Selected Factors

Presence of remote infection	Unadjusted rate, percent	Infection rate, percent, adjusted for: Classification of wound	Duration of operation	Age	Preoperative hospitalization	Urgency of operation	Diabetes	Steroid therapy	Obesity	Malnutrition
No	6.7	6.8	6.8	6.8	6.7	6.8	6.8	6.8	6.8	6.7
Yes	18.4	15.0	19.2	18.1	17.2	16.8	18.3	18.3	18.1	18.0
Total	7.4									

Table 36. Incidence of Infection, by Selected Factors, Unadjusted and Adjusted for Presence of Remote Infection

Preoperative hospitalization			Duration of operation			Urgency of operation		
Days	Crude rate, percent	Adjusted rate, percent	Hours	Crude rate, percent	Adjusted rate, percent	Operation	Crude rate, percent	Adjusted rate, percent
0-1	6.0	6.1	½	3.6	4.1	Elective	6.7	6.6
2-6	7.3	7.2	½ - 1	5.9	6.3	Urgent	11.7	10.8
7-13	9.1	9.0	1 - 2	6.4	6.4	Emergency	12.1	11.5
14-20	11.0	9.8	2 - 3	9.0	8.9			
21-	14.7	14.0	3 - 4	10.0	9.6			
Outpatient	3.0	2.9	4 - 5	10.9	10.2			
			5 - 6	15.4	15.0			
			6 -	17.6	17.4			

Classification of wound			Age of patient			Metabolic & nutritional factors		
Classification	Crude rate, percent	Adjusted rate, percent	Years	Crude rate, percent	Adjusted rate, percent	Factor	Crude rate, percent	Adjusted rate, percent
Clean	5.1	5.1	1	5.2	5.4	Diabetes	10.4	9.9
Clean-contaminated	10.8	10.4	1-14	4.8	5.2	Steroid		
Contaminated	16.3	15.5	15-24	4.7	4.9	therapy	16.0	15.2
Dirty	28.6	26.1	25-34	5.5	5.6	Obesity	18.1	17.1
			35-44	5.9	6.1	Malnutrition	22.4	19.2
			45-54	7.5	7.4			
			55-64	9.4	9.2			
			65-74	10.7	10.2			
			75-	9.2	8.5			

the patient that would predispose him to wound infection or by the nature or duration of the operation. The relationship between remote infection and wound infection may be explained by any of several general hypotheses.

1. The presence of remote infection may merely indicate a higher degree of susceptibility of a patient to all infectious processes owing to low general host resistance. Arguing against this is the observation in this study (Table 35, 36) that the specific factors believed to correlate with poor host resistance—age, diabetes, steroid therapy, malnutrition, and obesity—do not correlate with the presence of remote infection.

2. The initial infection may itself lower the patient's resistance, making him more susceptible to a subsequent wound infection. Dineen (1961) suggested a lowered state of general host resistance as the best explanation for his observation that patients undergoing second operative procedures had a greater infection rate than patients undergoing primary operations. More specific processes may also depress the host's resistance to subsequent infection, such as the phenomenon of acquired hypersensitivity. Johnson, Cluff, and Goshi (1961) noted a greater susceptibility to staphylococcal infections in rabbits previously infected with staphylococci, and showed that this altered host response was due to hypersensitivity that could be induced by the antigenic action of suspensions of the killed organisms.

3. Many of the wound infections in the patients with pre-existing remote infections may result from autogenous contamination of the wound site. Knight and Collins (1955) noted that patients with staphylococcal furunculosis were predisposed to staphylococcal wound infections. Further evidence of the autogenous origin of some wound infections is the work of Ketcham and co-workers (1962, 1963), who showed by phage-typing that strains of staphylococci isolated preoperatively from skin lesions or operatively from necrotic tumor frequently caused wound sepsis postoperatively. Howe and Marston (1962) used similar technics to document autogenous wound infection. An extension of the concept that the patient may infect his own wound from another site of infection was proposed by Williams *et al.* (1959): the patient who is an asymptomatic nasal carrier of coagulase-positive staphylococci should be regarded as harboring subclinical infection capable of infecting the operative wound with the same organisms. The increased risk of autogenous staphylococcal wound infection in such nasal carriers has been well documented by those authors and by others (Weinstein, 1959b; Ketcham *et al.*, 1963).

Whatever its cause, the strikingly high wound infection rate in patients with remote infections deserves further study.

Local Wound Factors

Although a few military surgeons, such as Ambrose Paré, had noted that traumatic wounds healed with less inflammation if gently cleansed than if treated with the customary application of boiling oil, Kocher was the first modern surgeon to extend these observations to elective incisions. He showed that careful hemostasis and gentle handling of incised tissue was attended by a lowered rate of wound sepsis. Kocher's views were adopted by Halsted, and the principles which he emphasized—complete hemostasis, adequate blood supply, absence of devitalized tissue, obliteration of dead space, use of fine nonabsorbable suture material, and wound closure without tension—are widely applied today to promote primary wound healing and to minimize the risk of wound infection.

The importance of the condition of the local wound in relation to wound healing and infection was summarized by Reid (1936). Meleney (1935) documented these clinical impressions when he reported an increased infection rate in wounds that developed hematomas. He also presented evidence to support his conviction that the use of silk for ligatures and sutures was followed by a lower infection rate than the use of catgut. More recent experimental work has shown that, with standard degrees of bacterial contamination, the local tissue condition may be decisive in preventing or promoting wound infection. Miles and his co-workers (1957) demonstrated that ischemia, whether induced by systemic shock or by local adrenalin, greatly enhanced the infectivity of bacteria, and that local injections of heparin produced a similar effect. Goshi and associates (1961) have shown that the presence of necrotic tissue enhances experimental staphylococcal infection in rabbits. Using quantitative bacteriological technics with human volunteers, Elek (1956) demonstrated that the pathogenicity of a strain of *Staphylococcus aureus* could be increased ten-thousandfold by the presence of a foreign body, such as a silk suture. Perhaps related to these experimental findings is the observation by Lidwell (1961) that length of operative incision influenced wound infection rate, with long incisions becoming infected more frequently than short ones.

In the present study, the method of closure of the operative wound and the type of operative drainage, if any, were regarded as *local wound factors* that might influence infection rate. In addition to simple physical exposure, drained or open wounds are certainly more likely to undergo postoperative bacterial contamination than undrained or primarily closed wounds. However, because of the different clinical situations involved, the infection rates for various methods of closure and drainage must be examined closely for comparability of the groups, to permit statistical adjustment of any disparity in composition of the groups.

Closure. Operative closure of the incision was classified as, 1) primary closure; 2) secondary closure; 3) none or incomplete closure; 4) skin graft; or 5) other. The infection rates for the different modes of closure are listed in Table 37.

As one would expect, higher infection rates were found in wounds closed secondarily and unclosed or partially closed than in wounds primarily closed. The significantly higher infection rates in the wounds that were not closed primarily is not, of course, proof that method of closure itself determines incidence of infection. As every surgeon knows, certain operative situations, such as encountering frank pus, dictate the methods of closure and wound drainage. A concentration of contaminated and dirty cases in the group of wounds not closed primarily would adversely affect the infection rate for the method of closure used. Wound classification, duration of surgery, and urgency of surgery have been tabulated against the method of wound closure and infection rate (Tables B-21–

B-23). Infection rates for method of closure adjusted for these factors have been calculated from those tabulations and are summarized in Table 38.

From Table B-21 the infection rates by type of closure were adjusted for operative contamination as indicated by wound classification.* Adjustment markedly narrows the difference between the rates of primarily closed incisions and incisions not closed or only incompletely closed (Fig. 16). The infection rate for secondary closures is not greatly changed by adjustment, however, and the rates for all varieties of closure are only slightly affected by adjustment for duration or urgency of operation. Individual hospital infection rates are given for the various types of wound closure in Table B-47 and the rates for each type of closure were adjusted for hospital differences. Again, the adjusted rates do not vary greatly from the unadjusted rates.

Discussion: The 95.0 per cent of all incisions that were closed primarily had an infection rate of 7.0 per cent, and the 2.6 per cent not closed or incompletely closed had an infection rate of 15.2 per cent. That this difference in infection rates is largely due to the greater number of nonclean operations that were not closed or incompletely closed can be shown by using the direct method of adjustment to calculate infection rates for the two kinds of closure, corrected for differences in classification of wound subjected to each. The adjusted infection rates are 10.0 per cent for primarily closed wounds and 11.9 per cent for wounds not closed or incompletely closed. The residual difference between the two adjusted infection rates may be due in part to the opportunity for postoperative bacterial contamination in wounds not closed primarily. Howe and Marston (1962) have presented evidence that such open wounds may become infected by postoperative cross-contamination on the ward.

The high infection rate for wounds closed secondarily (presumably, the most favorable of those wounds left open) is of interest, because it is even higher than the rate for wounds left completely or partially open.

It is concluded that, although the infection rate for wounds left open or incompletely closed is more than twice that for wounds closed primarily, the difference is largely explained by the greater proportion of contaminated wounds in the unclosed or incompletely closed group. It is believed that the degree of operative contamination was a prominent factor in the surgeon's selection of method of closure, and that the selection of wounds rather than method of closure played the dominant role in determining the infection rate.

Drains. The method of drainage of the operative wound at the time of closure was classified as, 1) no drains; 2) subcutaneous drain brought out through in-

* Refined-clean wounds were excluded from the adjustments because they were by definition closed primarily.

Table 37. Incidence of Infection, by Type of Operative Closure

Type of closure	Wounds		
	Number of wounds	Number of infections	Infection rate, percent
Primary	14,836	1,032	7.0
Secondary	39	11	28.2
None or incomplete	402	61	15.2
Skin graft	221	38	17.2
Other	36	12	33.3
Unknown	79	3	3.8
Totals	15,613	1,157	7.4

Table 38. Incidence of Infection, by Type of Operative Closure, Unadjusted and Adjusted for Selected Factors

Type of closure	Unadjusted infection rates, percent	Infection rates, percent, adjusted for		
		Classification of wound*	Duration	Urgency
Primary	7.0	10.0	7.0	6.9
None or incomplete	15.2	11.9	14.6	14.5
Secondary	28.2	24.5	24.0	28.4
Totals	7.4	10.4	7.4	7.4

*Excluding refined-clean wounds.

Drains. The method of drainage of the operative wound at the time of closure was classified as, 1) no drains; 2) subcutaneous drain brought out through in-

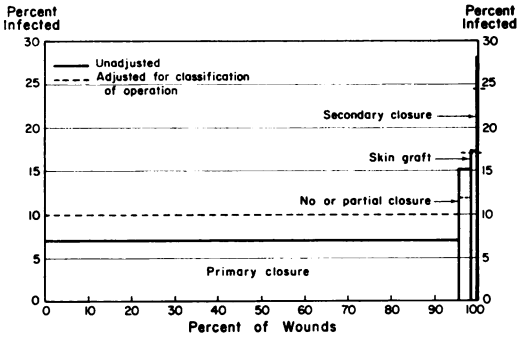

FIG. 16. Percentage of wounds infected, by type of closure.

cision; 3) drain from serous cavity brought out through incision; 4) drain, subcutaneous or from serous cavity, brought out at a site remote from incision; or 5) other. Table 39 lists the infection rates for the various methods of drainage.

It is apparent from Table 39 that all methods of drainage (except the *other*, which accounted for a negligible three wounds) were associated with similar infection rates, which ranged from 11.3 to 12.0 per cent, compared with the nondrained wounds, of which only 5.0 per cent became infected.

Method of drainage, like method of closure, is often dictated by the operative situation, and one would expect to find among the drained group more contaminated and dirty wounds, perhaps more urgent and emergency operations, and perhaps longer operations. Tables B-24—B-26 list infection rates by method of drainage, wound classification, and urgency and duration of operation. Table 40 presents the infection rates for drained and nondrained wounds adjusted for those factors.

When adjustment for operative contamination, as revealed by wound classification,* is made, the marked difference between the crude infection rates for drained and nondrained wounds is somewhat diminished (Fig. 17). Adjustments for duration and urgency of operation do not produce important changes.

Discussion: It appears that the markedly higher infection rate for drained wounds, 11.1 per cent, than for nondrained wounds, 5.0 per cent, is largely independent of wound classification; that is, the greater concentration of nonclean wounds in the drained group is responsible for only a small portion of the difference in infection rates between the two groups. This difference is also independent of duration and urgency of operation and hospital differences. Meleney (1935) and Lidwell (1961) also noted a higher infection rate for drained than for nondrained wounds, although neither author implied that drained and nondrained wounds were comparable in all other respects.

*Refined-clean wounds were excluded from the adjustments because they were by definition nondrained.

Table 39. Incidence of Infection, by Type of Drain

Type of drain	Number of wounds	Number of infections	Infection rate, percent
No drain	9,447	474	5.0
Subcutaneous, drained through wound	3,014	346	11.5
Serous cavity, drained through wound	1,422	171	12.0
Remote drain	2,042	230	11.3
Other	3	0	0.0
Unknown	58	5	8.6
Totals	15,613*	1,157	7.4

*For some incisions more than one drain site was provided, so that sum of wounds and infections in all categories exceeds the total numbers of wounds studied and infections observed.

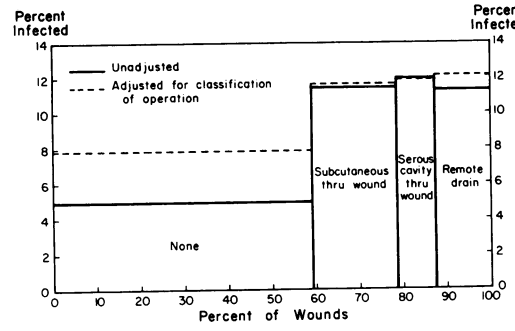

FIG. 17. Percentage of wounds infected, by type of drain provided.

Table 40. Incidence of Infection, by Type of Drain, Unadjusted and Adjusted for Selected Factors

Type of drain	Unadjusted infection rates, percent	Infection rates, percent, adjusted for Classification of wound*	Duration of operation	Urgency of operation
No drain	5.0	7.9	5.4	5.0
One or more	11.1	12.1	10.6	11.1
Subcutaneous wound	11.5	13.6	11.2	11.4
Serous cavity wound	12.0	11.9	12.6	11.8
Remote	11.3	12.1	11.6	11.6
Totals	7.4	10.4	7.4	7.4

*Excluding refined-clean wounds.

It is interesting that the depth and position of the drain in relation to the operative incision made little difference in the wound infection rate.

It is concluded that the high infection rate for drained wounds, more than twice that for undrained wounds, cannot be entirely explained on the basis of operative contamination or duration or urgency of operation, at least within the limits of our protocol. Although one may speculate on the role of the drain as a source of postoperative contamination of the wound, other factors may be responsible for the infection rates. A surgeon may choose to drain a given operative incision if further bleeding is likely or if he believes that there may be subsequent leakage of intestinal contents, bile, or urine into the wound. Predictions of what will occur in the course of wound healing entail evaluations of such very real factors as the degree of hemostasis obtained and the reliability of a suture line. These factors, which are apparent to the surgeon when he decides to drain or not to drain, must certainly influence infection rates, although they are too subtle to be isolated by such categories as wound classification or duration or urgency of operation. No conclusions can be reached indicting the drain as a cause of wound infection, although a higher infection rate is noted in those wounds which are drained.

Other Operative Factors.

This section considers the relationship of wound infection rate to four characteristics of the operative procedure: duration, urgency, time of day, and month. Whereas previous sections dealt with factors related to the three major aspects of the genesis of wound infection—bacterial contamination of the wound, general host resistance, and local wound factors—the operative characteristics considered here are more complex and may well influence wound infection rate through a combination of those primary factors. For example, the increased infection rate evidently associated with long operations might result from increased bacterial contamination of the wound at operation, *or* from the detrimental effect of the stress of prolonged anesthesia and blood loss on the patients' general resistance, *or* from the unfavorable effect of exposure and trauma on the deep tissues of the wound itself. Although the specific

Table 41. Incidence of Infection, by Duration of Operation

Duration of operation, minutes	Number of wounds	Number of infections	Infection rate, percent
0- 29	1,340	48	3.6
30- 59	3,055	181	5.9
60-119	5,671	363	6.4
120-179	2,806	253	9.0
180-239	1,295	129	10.0
240-299	651	71	10.9
300-359	337	52	15.4
360 or more	267	47	17.6
Unknown	191	13	6.8
Totals	15,613	1,157	7.4

way in which duration of operation influences wound infection rate is not clear, the knowledge that a relationship exists is nonetheless valuable as a guide in estimating the risk of sepsis in a given procedure.

Duration of Operation. At the completion of each operative procedure, the length of the operation in minutes was recorded. The various durations were then grouped by half-hour or one-hour increments, and the infection rates were calculated (Table 41). As the duration of operation increases, a progressive increase in the infection rate is manifested (Fig. 18). Furthermore, this relationship is demonstrated rather consistently in the experience of each of the five hospitals (Table 42).

Duration of operation itself may not be responsible for the higher infection rates in the more time-consuming operations. For example, it may be that operations with contamination from the gastro-intestinal tract take longer than clean procedures on more superficial structures, and that a high infection rate after long operations merely reflects the greater incidence of nonclean operations in that group. However, Tables 43 and B-27, which show the relationship of wound classification to duration of operation and infection rate, reveal that refined-clean wounds and all clean wounds also show a progressive increase in infection rate with increasing duration of operation.

Further evidence that duration of operation influences infection rates independently is obtained by adjusting the duration-of-operation—specific rates for wound classification, age, metabolic and nutritional state, urgency of operation, and duration of preoperative hospitalization. The adjusted rates are in Tables B-3, B-12, and B-27–B-29, and summarized in Table 43, and can be seen to change the marked effect of duration of operation on wound infection rate only slightly.

It is of interest to examine the effect of duration of operation on the separate infection rates of ultraviolet irradiated and unirradiated (control) wounds (Table 44). Irradiation did not alter the steady increase in infection rate with duration of operation.

Discussion: Evidence has been presented to show that wound infection rate is influenced by duration of operation. This association was also noted by British investigators (Public Health Laboratory Service, 1960). In a statistical analysis of their study, Lidwell (1961) concluded that the

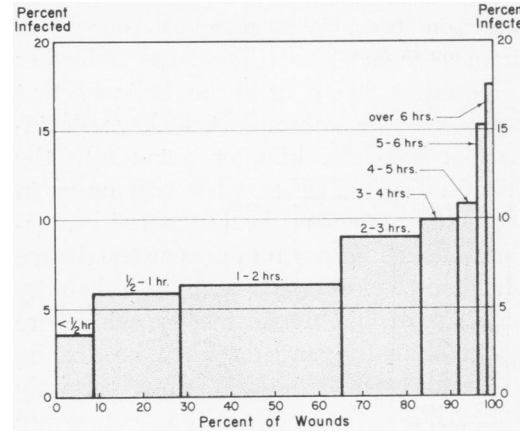

FIG. 18. Percentage of wounds infected, by duration of operation, in hours.

Table 42. Incidence of Infection, by Duration of Operation and Hospital

Duration of operation, minutes	Infection rate, percent						
	Combined hospitals	Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5	Adjusted for hospital differences
0 - 29	3.6	1.5	5.9	4.8	3.1	3.4	3.8
30 - 59	5.9	3.8	6.5	8.5	3.3	6.7	6.0
60 - 119	6.4	3.5	5.7	10.4	2.2	8.8	6.6
120 - 179	9.0	5.2	8.5	11.0	4.0	12.8	9.1
180 - 239	10.0	7.7	10.2	15.5	3.0	10.2	9.5
240 - 299	10.9	11.4	9.4	12.7	4.0	14.6	11.1
300 or more	16.4	22.4	12.2	22.3	5.4	20.5	17.1
Totals	7.4	4.8	7.0	11.7	3.0	8.8	

duration of the operative procedure influenced the infection rate independently of the other factors analyzed, a conclusion that appears substantiated by the results of the present study.

One may only speculate on the manner in which increasing duration of operation results in increasing incidence of infection, but it could occur in any, or a combination, of several ways.

1. The total bacterial contamination of the incision may well increase with time, whether by the airborne route, by exogenous contact, or by endogenous spread.

2. The combined effects of exposure of the wound to air, trauma from prolonged retraction and manipulation, and presumably increased amounts of suture material left at the operative site result in a local wound condition that may become more and more favorable for infection as length of operation increases.

3. Long procedures often expose more tissue than short procedures, which might accentuate both the increasing total bacterial contamination of the incision and the deteriorating local wound resistance.

4. In longer procedures, the opportunity for systemic insult to the patient, through blood loss or otherwise, is generally greater than in shorter procedures, which may be reflected in a diminished general resistance to infection.

The striking relationship noted between increasing duration of operation and increasing infection rate appears to be independent of other factors known to influence infection rate and may be assumed to be of primary importance.

Urgency of Operation. Operative procedures were recorded as, 1) elective; 2) urgent; or 3) emergency. For the purposes of this study, procedures were considered

Table 43. Incidence of Infection, by Duration of Operation, Unadjusted and Adjusted for Selected Factors

Duration of operation, minutes	Infection rates, percent											
	Unadjusted			Adjusted for								
	Refined-clean wounds	All clean wounds	All wounds	Class of wound	Age	Diabetes	Steroid therapy	Obesity	Malnutrition	Urgency	Pre-operative stay	Hospital
0 - 29	1.7	2.3	3.6	4.2	3.9	3.5	3.7	3.6	3.6	4.0	4.5	3.8
30 - 59	2.7	3.6	5.9	6.3	6.2	5.9	5.9	5.9	5.9	5.9	6.1	6.0
60 - 119	2.9	4.5	6.4	6.6	6.5	6.3	6.3	6.4	6.3	6.3	6.4	6.6
120 - 179	4.7	6.2	9.0	8.6	8.8	9.0	9.0	9.0	9.0	9.0	10.1	9.1
180 - 239	6.1	8.7	10.0	9.3	9.5	10.2	10.1	9.9	9.9	10.2	10.2	9.5
240 - 299	5.8	10.1	10.9	10.0	10.5	10.8	10.9	10.9	10.9	10.8	11.0	11.1
300 - 359	13.3	16.3	15.4	15.3	13.4	15.5	15.6	15.7	15.5	15.5	15.0	16.6
360 or more	14.5	12.1	17.6	15.0	15.0	17.7	16.1	17.7	17.2	17.7	14.7	17.7
Not reported	1.8	3.0	6.8									
Total	3.3	5.1	7.4									

Table 44. Incidence of Infection, by Duration of Operation and Treatment Status

Duration of operation, minutes	Ultraviolet			Control		
	Number of wounds	Number of infections	Infection rate, percent	Number of wounds	Number of infections	Infection rate, percent
0- 29	641	25	3.9	699	23	3.3
30- 59	1,507	97	6.4	1,548	84	5.4
60-119	2,733	175	6.4	2,938	188	6.4
120-179	1,372	117	8.5	1,434	136	9.5
180-239	649	64	9.9	646	65	10.1
240-299	312	32	10.3	339	39	11.5
300-359	170	27	15.9	167	25	15.0
360 or more	116	19	16.4	151	28	18.5
Unknown	94	3	3.2	97	10	10.3
Totals	7,594	559	7.4	8,019	598	7.5

elective if they were electively scheduled; urgent procedures were defined as those not electively scheduled, but for which a delay of operation of 12 hours or more was considered permissible; and emergency procedures were those in which operation could not be delayed for 12 hours.

The influence of urgency of operation on infection rate is summarized in Table 45. The high infection rates for nonelective operations may result not from the common factor of urgency alone, but from the contaminated nature of many of the nonelective procedures or from the susceptibility of patients undergoing nonelective surgery to infection by virtue of age or other conditions. This possibility is investigated by cross-tabulating infection rates by degree of urgency with other factors known or suspected to influence infection rate and factors that might be associated with urgency (Tables B-13, B-18, B-22, B-26, B-28, and B-30).

Table 45. Incidence of Infection, by Urgency of Operation

Urgency of operation	Number of wounds	Number of infections	Infection rate, percent
Elective	13,183	877	6.7
Urgent	846	99	11.7
Emergency	1,334	161	12.1
Unknown	250	20	8.0
Totals	15,613	1,157	7.4

Inspection of Table B-30 reveals that 57.1 per cent of the nonelective cases (urgent and emergency) were classified as nonclean, whereas only 19.3 per cent of the elective procedures were classified as nonclean. Infection rates for elective, urgent, and emergency surgery were therefore adjusted for classification of wound * and are presented in Table 46.

Adjustment for operative contamination, as indicated by wound classification, essentially eradicates the difference in infection rates between elective, urgent, and emergency procedures. Figure 19 illustrates the infection rates unadjusted and adjusted for urgency.

Adjustment for duration of operation, age, metabolic and nutritional factors, and

* Refined-clean wounds were excluded from the adjustments because they were by definition associated with elective surgery.

Table 46. Incidence of Infection, by Urgency of Operation, Unadjusted and Adjusted for Selected Factors

Urgency of operation	Infection rates, percent								
		Adjusted for							
	Unadjusted	Classification of wound*	Duration of operation	Age	Diabetes	Steroid therapy	Obesity	Malnutrition	Time of day
Elective	6.7	10.9	6.7	6.6	6.7	6.6	6.6	6.7	6.7
Urgent	11.7	10.7	11.1	11.3	11.5	11.7	11.8	11.7	12.2
Emergency	12.1	10.2	12.2	13.5	12.0	12.1	12.1	12.0	11.1
Totals	7.4	10.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4

*Excluding refined-clean.

time of day, however (Tables B-13, B-28, B-31, and B-32), produces only slight changes (Table 46).

Discussion: Dineen (1961) noted that emergency operations were attended by high infection rates but did not describe the composition of the group of patients undergoing emergency procedures. In the present study, both urgent and emergency procedures were associated with infection rates substantially higher than those for elective procedures. This difference appears to be explained entirely on the basis of operative contamination, rather than of any unique feature of urgency itself; when wound classification is adjusted for, the infection rates of elective and nonelective cases become practically identical. Thus, urgency itself is not a primary determinant of wound infection rate.

Time of Operation. The time was recorded at the beginning of each operative procedure as follows (in military time): 1) 0730-0939 hours; 2) 0930-1229 hours; 3) 1230-1529 hours; 4) 1530-2359 hours; or 5) 0000-0729 hours.

The lowest infection rate (6.5%) was noted (Table 47) for the beginning of the operating-suite work day (0730-0929), with a gradual rise in rate during the day to a peak in the evening shift (1530-2359), and an elevated rate still obtaining for the night shift (0000-0729).

Although such environmental factors as bacterial contamination of the air often change with time of day, thus influencing time-specific infection rates, the type of operation performed may also vary and may be responsible for the changing rates. The time-specific infection rates were cross-tabulated with urgency of operation and wound classification, and Tables B-32 and B-33 confirm the fact that the evening and night operative procedures included great concentrations of nonelective and nonclean cases. When the time-of-day—specific rates are adjusted for urgency and classification (Table 48), the trend of increasing infection rates from 0730 to 2359 becomes less marked; the remaining differences between time groups are small (Fig. 20), and display no pattern.

Discussion: The higher infection rates encountered in the later hours of the day appear to be explained almost entirely by

Table 47. Incidence of Infection, by Time of Beginning of Operation

Time operation began*	Number of wounds	Number of infections	Infection rate, percent
0730-0929	5,921	382	6.5
0930-1229	4,542	332	7.3
1230-1529	3,152	245	7.8
1530-2359	1,280	140	10.9
0000-0729	564	46	8.2
Unknown	154	12	7.8
Totals	15,613	1,157	7.4

*Military time.

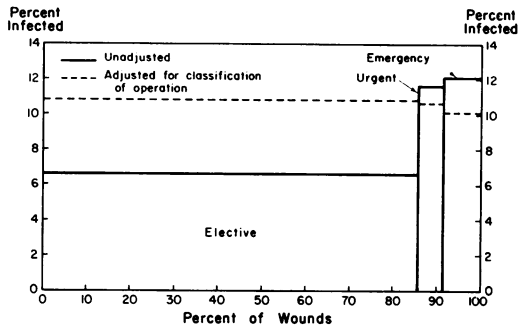

FIG. 19. Percentage of wounds infected, by urgency of operation.

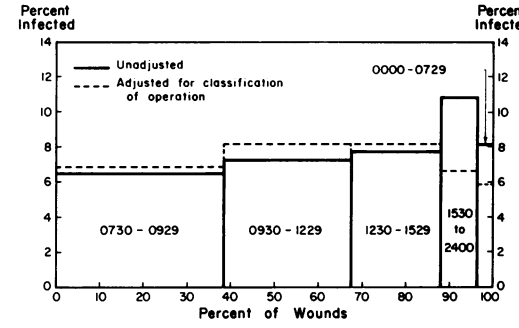

FIG. 20. Percentage of wounds infected, by time of day operation began.

the type of operative procedure performed. The disproportionately high number of nonclean and nonelective operations during the evening and night is apparently responsible for the high infection rates during those periods, and no such trend is seen for clean wounds. The time of day at which an operation begins cannot be considered a primary determinant of wound infection rate.

Month of Operation. Tables B-34 –B-37 list the infection rates by month for the combined hospitals and for the individual hospitals. These rates are shown graphically in Figures 21–26. Although the rates fluctuated from month to month, no seasonal trend is apparent, either in the combined experience or in individual hospitals. It was thought possible, however, that some small segment of the study population would demonstrate a trend that was obscured if the over-all population were studied as a whole. Therefore, infection rates by month were examined separately for ultraviolet and control rooms (Fig. 27), for all refined-clean wounds (Fig. 28), and for those clean and refined-clean operations performed in the control rooms (Fig. 29, 30). There was still no apparent seasonal trend.

Table 48. Incidence of Infection, by Time of Beginning of Operation, Unadjusted and Adjusted for Selected Factors

Time operation began*	Infection rates, percent				
	Unadjusted			Adjusted for	
	Elective operations	Clean operations	All operations	Urgency	Wound classification
0730-0929	6.2	5.2	6.5	6.9	6.9
0930-1229	6.8	5.0	7.3	7.6	8.2
1230-1529	7.2	5.0	7.8	7.9	8.2
1530-2359	7.4	5.3	10.9	8.0	6.7
0000-0729	7.2	6.0	8.2	7.3	5.9
Totals	6.7	5.1	7.4		

*Military time.

Discussion: Seasonal peaks in infection rates have been noted in previous studies. Dineen and Pearce (1958) found that over a 10-year period the number of staphylococcal wound infections increased during March and December. A seasonal increase was described by Hart with Gardner (1937) and Upchurch (1941) as occurring in the colder months at Duke Hospital, before ultraviolet lamps were installed in the operating rooms. Hart ascribed the phenomenon to the well-documented seasonal changes in the bacterial population of the operating-room air, particularly for *Staph. aureus.* Similar observations of seasonal outbreaks of hemolytic streptococcus wound infections had been made even earlier (Meleney, 1927; Walker, 1930), but Meleney noted (1935) that the use of surgical masks in the operating room obliterated such seasonal trends.

In the present study, the infection rates for the winter months, December, January, and February, were no higher than the over-all infection rate for the 27-month period. This is true even for the refined-clean procedures performed in the control operating rooms; that group might be expected to show an increased infection rate if an epidemiological situation similar to that at Duke Hospital in the pre-ultraviolet years (characterized by a high clean-case infection rate, most probably associated with airborne contamination, increasing in the winter months) were present in the study hospitals. Such epidemiological differences offer a partial ex-

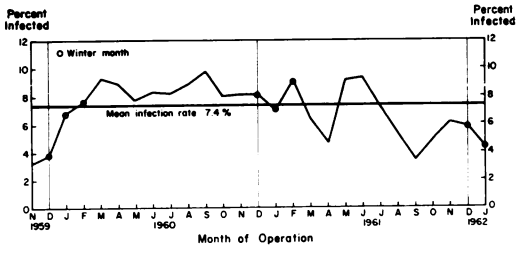

FIG. 21. Percentage of wounds infected, by month, all hospitals combined.

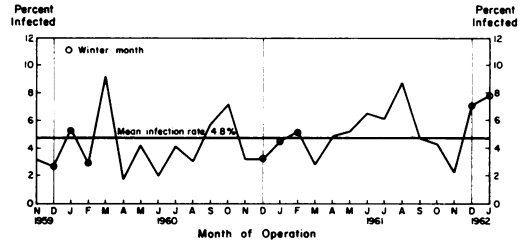

FIG. 22. Percentage of wounds infected, by month, Hospital 1.

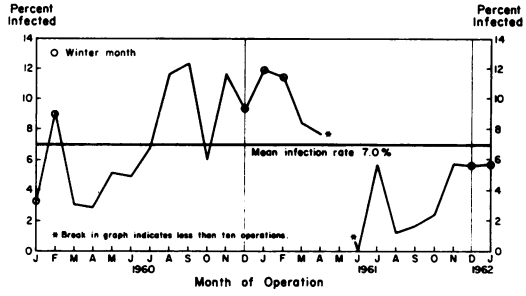

FIG. 23. Percentage of wounds infected, by month, Hospital 2.

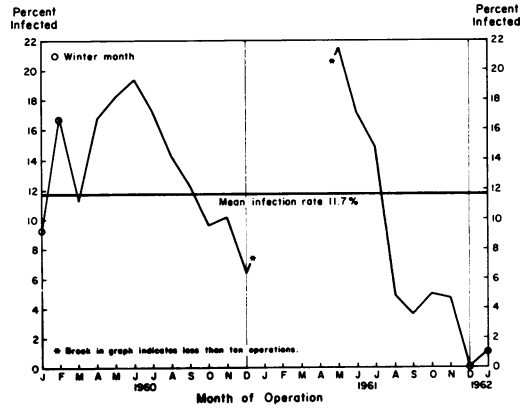

FIG. 24. Percentage of wounds infected, by month, Hospital 3.

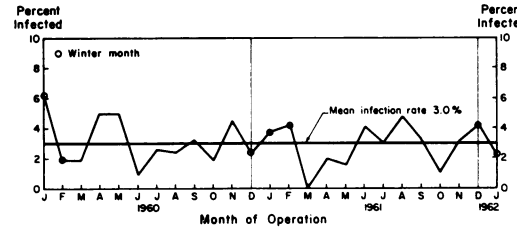

FIG. 25. Percentage of wounds infected, by month, Hospital 4.

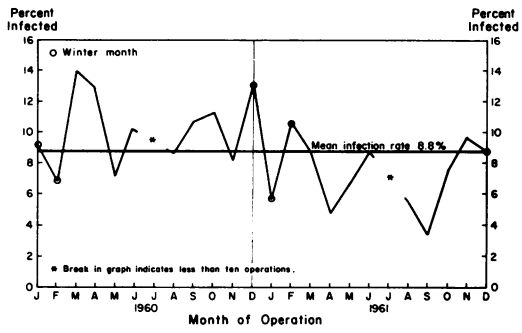

FIG. 26. Percentage of wounds infected, by month, Hospital 5.

planation as to why the results of ultraviolet irradiation in this study were less impressive than those found by Hart.

Preoperative and Postoperative Factors

Duration of Preoperative Hospitalization. The elapsed time between hospital admission and operation was recorded for each patient as, 1) 0 to 1 day; 2) 2 to 6 days; 3) 7 to 13 days; 4) 14 to 20 days; or 5) 21 days or more. If he was an outpatient, that was recorded.

The incidence of infection according to preoperative hospitalization is presented in Table 49 and Figure 31. A steady increase in the incidence of infection is noted with increasing preoperative hospitalization. Table 50 presents the combined and individual hospital infection rates for preoperative hospitalization. The same steady increase is noted in every institution except Hospital 4, where the trend is less regular.

It may be asked whether the apparent relationship of infection rate to duration of preoperative hospitalization reflects something intrinsically detrimental about being in a hospital environment for a prolonged period, or simply exists because of a heavy concentration of aged or debilitated patients about to undergo more formidable types of operation. Tables B-5, B-14, B-20, B-29, B-44, and B-48 give the

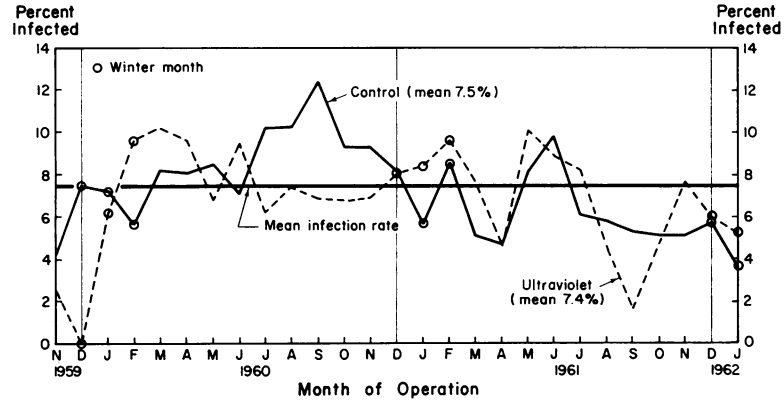

FIG. 27. Percentage of wounds infected, by month and treatment status.

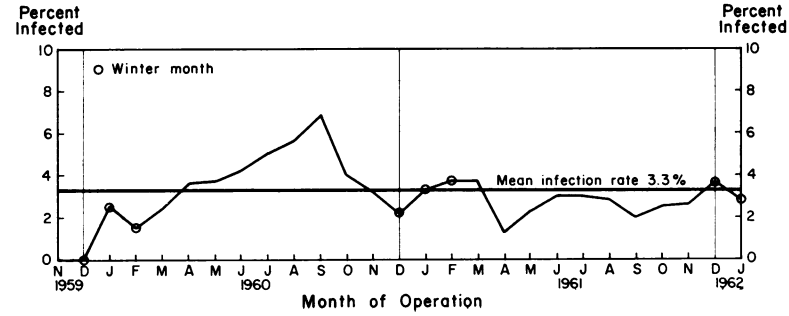

FIG. 28. Percentage of wounds infected, by month, refined-clean operations.

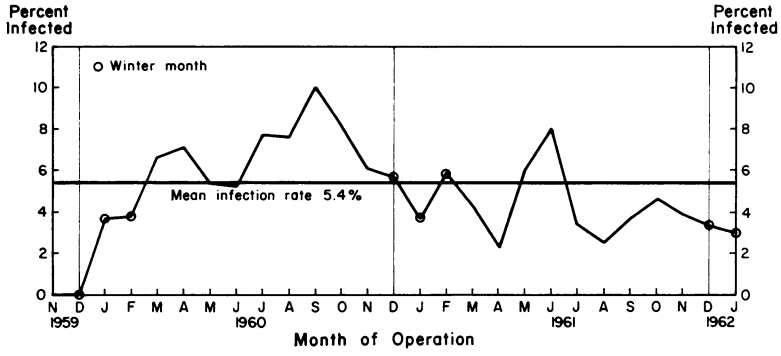

FIG. 29. Percentage of wounds infected, by month, for control (non-UV) wounds, all clean operations.

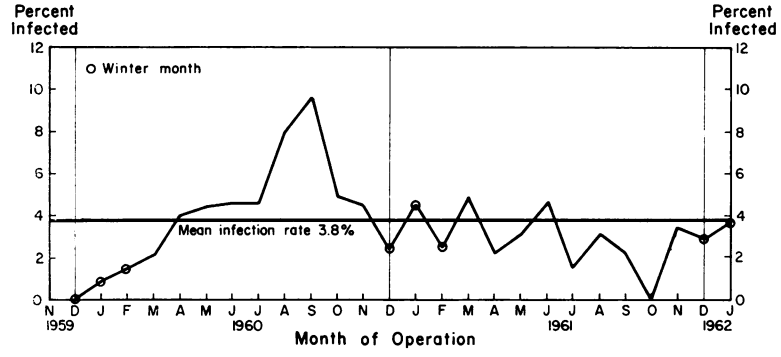

FIG. 30. Percentage of wounds infected, by month, for control (non-UV) wounds, refined-clean operations.

infection rates for preoperative hospitalization cross-tabulated for age, specific metabolic and nutritional factors, remote infection, wound classification, duration of operation, and hospital. Infection rates for duration of preoperative hospitalization were adjusted for these factors (Table 51). Although patients with specific metabolic and nutritional problems tended to be hospitalized preoperatively for longer periods (Table B-14), adjustment does not greatly alter the rates for duration of preoperative stay. Similarly, adjustments for the slight increase of elderly patients, for the increased length of operations, and so on, result in only slight modification of the trend evident in the unadjusted rates.

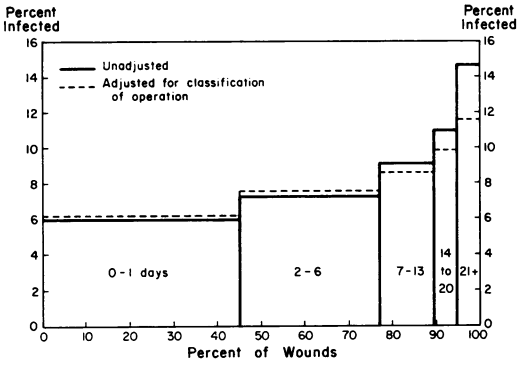

FIG. 31. Percentage of wounds infected, by duration of preoperative hospitalization, in days.

Table 49. Incidence of Infection, by Duration of Preoperative Hospitalization

Preoperative stay, days	Number of wounds	Number of infections	Infection rate, percent
0- 1	6,783	405	6.0
2- 6	4,820	354	7.3
7-13	1,932	176	9.1
14-20	746	82	11.0
21 or more	773	114	14.7
Outpatient	403	12	3.0
Unknown	156	14	9.0
Totals	15,613	1,157	7.4

Table 50. Incidence of Infection, by Duration of Preoperative Hospitalization and Hospital, Unadjusted and Adjusted for Hospital

Preoperative stay, days	Infection rates, percent						
	Unadjusted						Adjusted for hospital
	Combined hospitals	Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5	
Outpatient	3.0	0.0	6.3	0.0	0.0	1.8	1.8
0- 1	6.0	3.3	4.9	8.8	3.0	7.8	6.0
2- 6	7.3	6.0	6.2	13.5	1.7	8.5	7.4
7-13	9.1	8.1	8.0	19.7	2.6	10.3	9.8
14-20	11.0	9.7	13.4	22.0	4.3	12.1	12.3
21 or more	14.7	15.9	24.4	22.4	6.0	20.6	18.5
Unknown	9.0	4.0	0.0	10.7	0.0	17.6	
Totals	7.4	4.8	7.0	11.7	3.0	8.8	

Discussion: The increase of infection rate with length of preoperative hospitalization is not explained within the limits of this study, on the basis of association of the specific patient factors or the specific operative factors known to exert a major influence on wound infection rate. A similar trend was noted in a survey of wound infections in England and Wales (Public Health Laboratory Service, 1960). There are two possible explanations of the relationship of preoperative hospitalization to infection rate.

1. There may be specific patient characteristics other than age, diabetes, steroid therapy, obesity, and malnutrition that, although unrecognized, predispose the patient to infection and at the same time are associated with prolonged preoperative hospitalization. A corollary of this hypothesis is that certain operative factors other than duration of operation and wound classification are present but unrecognized and directly influence both duration of preoperative stay and incidence of wound infection. Although such patient or operative characteristics obviously may exist, they are often not readily discernible.

2. Preoperative hospitalization itself may directly affect susceptibility to infection, either by lowering host resistance factors, or by providing

Table 51. Incidence of Infection, by Duration of Preoperative Hospitalization, Unadjusted and Adjusted for Selected Factors

Preoperative stay, days	Infection rates, percent								
		Adjusted for							
	Unadjusted	Age	Diabetes	Steroid Therapy	Obesity	Malnutrition	Duration of operation	Classification of wound	Hospital
Outpatient	3.0	3.0	*	*	*	*	11.2	3.0	1.8
0- 1	6.0	6.4	5.9	5.9	5.9	6.0	6.7	6.2	6.0
2- 6	7.3	7.1	7.2	7.3	7.3	7.3	6.9	7.6	7.4
7-13	9.1	8.8	8.9	8.9	9.0	9.0	8.2	8.6	9.8
14-20	11.0	10.9	11.0	10.7	11.0	10.7	11.0	9.9	12.3
21 or more	14.7	13.7	14.8	14.8	14.8	14.9	14.7	11.6	18.5
Totals	7.4								

*Fewer than 10 patients with specific patient factors.

Table 52. Incidence of Use of Prophylactic Antibiotics, by Hospital and in Relation to Certain Patient and Operative Factors Known to Influence Infection Rates

Factor	Number of wounds	Prophylactic antibiotics: No. of wounds for which used	Prophylactic antibiotics: Incidence of use, percent
Class of wound			
Refined-clean	6,264	875	14.0
Other clean	4,989	1,538	30.8
Clean-contaminated	2,575	1,437	55.8
Contaminated	670	377	56.3
Dirty	577	379	65.7
Diabetes			
With	354	156	44.1
Without	14,664	4,420	30.1
Steroid Therapy			
With	119	56	47.0
Without	14,899	4,520	30.3
Obesity			
With	165	66	40.0
Without	14,853	4,510	30.4
Malnutrition			
With	66	41	62.1
Without	14,952	4,535	30.3
Hospital			
1	2,329	665	28.6
2	2,847	429	15.1
3	2,527	950	37.6
4	2,562	911	35.6
5	4,879	1,687	34.6
Duration of operation			
> 30 min	1,114	130	11.7
30- 59 min	2,905	474	16.3
60-119 min	5,626	1,482	26.3
120-179 min	2,788	1,097	39.3
180-239 min	1,289	657	51.0
240-299 min	644	370	57.5
300-359 min	335	210	62.7
360 min or more	264	190	72.0
Duration of preoperative hospitalization			
Under 2 days	6,763	1,399	20.7
2-6 days	4,790	1,736	36.2
7-13 days	1,927	793	41.2
14-20 days	745	321	43.1
21 days or more	768	334	43.5
Urgency of operation			
Elective	12,741	3,424	26.9
Urgent	840	437	52.0
Emergency	1,319	690	52.3
Total experience*	15,144	4,642	30.7

*Excludes patients for whom antibiotic status not known.

increased opportunity for ultimate bacterial contamination of the wound. Knight and co-workers (1957, 1958) have shown that hospitalized patients gradually become colonized with antibiotic-resistant staphylococci and that therapy with tetracycline or penicillin greatly accelerates the process. Williams *et al.* (1959) also noted that increased duration of hospitalization was related to a greater proportion of nasal carriers of coagulase-positive staphylococci; he also described an increased wound infection rate in such nasal carriers of pathogenic staphylococci, a finding confirmed by the work of Ketcham and associates (1962, 1963). Such evidence nicely supports the hypothesis that the increased infection rate in patients with prolonged preoperative hospitalization is related to the higher proportion of nasal carriers of coagulase-positive staphylococci in this group. Still unexplained in this hypothetical sequence of events is the final common pathway of the resident organisms to the operative wound.

The association of wound infection rate with duration of preoperative hospitalization is impressive and appears to be at least partially independent of the other operative or patient factors examined in this study. The possibility of bias, beyond that recognized and adjusted for in the comparisons, is so real as to deter the authors from a more definite conclusion. The underlying cause of the relationship and its practical implications merit further investigation.

Prophylactic Antibiotics. Prophylactic antibiotics were defined as those administered in the absence of or before infection and were distinguished from therapeutic antibiotics used to treat an established infection. The frequency with which antibiotics are administered varies widely with many factors; as a result, the incidence of wound infection associated with their prophylactic use depends on several variables other than the use itself of a specific antibiotic. An analysis of the interrelationships between the prophylactic use of antibiotics, patient status, type of operation, and wound infection rate follows.

Prophylactic antibiotics were used to treat 4,642 wounds of the 15,144 wounds (30.7%) for which the status of antibiotic

coverage was known (Table 52). The incidence of use varied somewhat from hospital to hospital, from a low of 15.1 per cent (Hospital 2) to a high of 37.6 per cent (Hospital 3). Of the various antibiotics used, the most common was a combination of penicillin and streptomycin, used to treat 1,306 wounds, followed by chloromycetin (620 wounds), a combination of penicillin and tetracycline (556 wounds), tetracycline alone (517 wounds), penicillin alone (375 wounds), a combination of penicillin, streptomycin, and chloromycetin (249 wounds), and a combination of penicillin and chloromycetin (160 wounds). Other, less frequently used antibiotics and combinations were used for a total of 859 wounds. The use of a specific antibiotic or combination varied much more widely from hospital to hospital than did the incidence of use of prophylactic antibiotics in general. For instance, although the combination of penicillin and streptomycin was used for 1,036 wounds and was used more frequently than any other antibiotic or combination of antibiotics at four of the five hospitals, it was used only twice at Hospital 4. At Hospital 4, the combination of penicillin and tetracycline was most frequently used, being administered 541 times, whereas it was used a total of only 15 times at the other four hospitals. Over 60 per cent of the wounds treated with penicillin alone were in the group at Hospital 4, but over 80 per cent of the wounds treated with the combination of penicillin, streptomycin, and chloromycetin were at Hospital 5.

Table 52, derived from Tables B-38–B-43, compares the incidence of use of prophylactic antibiotics with certain operative factors and patient characteristics known to influence wound infection rate. For each of these factors, the groups of patients more likely to develop wound infection were more frequently given antibiotics prophylactically. This striking relationship, although not unexpected, demands cautious interpretation of the infection rates encountered in patients treated with prophylactic antibiotics.

The incidence of wound infection following the use of prophylactic antibiotics is greater than the infection rate of wounds in patients not treated with them. Table 53 and Figure 32 summarize the wound infection rate in patients treated and not treated with prophylactic antibiotics. In the total experience, the infection rate for the 4,642 wounds receiving prophylactic antibiotics was 14.3 per cent, in contrast with the 4.4 per cent infection rate of wounds not so treated. The higher infection rate asociated with prophylactic antibiotics is noted in every category of patient, operative characteristic, and hospital characteristic examined.

Comparison of Tables 52 and 53 reveals an interesting finding: the difference between the infection rates with and without prophylactic antibiotics was greatest in those groups that used them most sparingly. For example, only 14.0 per cent of the refined-clean wounds were treated with prophylactic antibiotics, but 65.6 per cent of the dirty wounds. The infection rates for refined-clean wounds with and without antibiotics were 9.4 and 2.3 per cent, respectively, for a ratio of 4.1:1, but for dirty wounds, the infection rates with and without were 31.7 and 22.2 per cent, for a ratio of only 1.4:1. Similarly, at Hospital 2, in which antibiotics were used prophylactically in only 15.1 per cent of the patients, the infection rates with and without were 27.5 and 3.5 per cent, for a ratio of 7.9:1, whereas in the over-all study experience, in which 30.7 per cent of the wounds received prophylactic antibiotics, the infection rates with and without were 14.3 and 4.4 per cent, for a ratio of only 3.2:1.

It has been shown that prophylactic antibiotics are more frequently given to patients who are poor risks, from the standpoint of susceptibility to infection (Table 52), and that a higher incidence of wound

Table 53. Incidence of Infection, by Use of Prophylactic Antibiotics and Selected Factors Known to Influence Infection Rates

Characteristic	Infection rate, percent: Prophylactic antibiotics used	Infection rate, percent: Prophylactic antibiotics not used
Class of wound		
Refined-clean	9.4	2.3
Other clean	11.7	5.4
Clean-contaminated	13.9	6.8
Contaminated	20.4	10.6
Dirty	31.7	22.2
Diabetes		
With	14.7	6.1
Without	14.3	4.4
Steroid therapy		
With	28.6	4.8
Without	14.2	4.4
Obesity		
With	24.2	14.1
Without	14.2	4.3
Malnutrition		
With	29.3	12.0
Without	14.2	4.4
Hospital		
1	10.4	2.5
2	27.5	3.5
3	16.1	9.1
4	5.8	1.5
5	16.1	5.4
Duration of operation		
> 30 min	13.8	2.3
30- 59 min	16.7	3.8
60-119 min	14.1	3.6
120-179 min	13.2	6.2
180-239 min	12.3	7.4
240-299 min	12.7	8.4
300-359 min	20.0	8.0
360 min or more	20.0	10.8
Duration of preoperative hospitalization		
Under 2 days	13.2	4.0
2-6 days	12.0	4.5
7-13 days	15.6	4.5
14-20 days	18.4	5.4
21 days or more	24.0	7.6
Urgency of operation		
Elective	13.4	4.3
Urgent	16.9	6.0
Emergency	17.5	6.0
Total experience	14.3	4.4

infection is associated with than without the administration of prophylactic antibiotics (Table 53). The question to be answered is whether the antibiotics themselves are responsible for the increased infection rate, or the increased rate simply reflects the poor-risk status of the group receiving them. The direct method of adjustment is used to compare infection rates for the group receiving antibiotics prophylactically and the group not receiving them (Table 54). Correction for the large proportion of nonclean wounds in the group receiving antibiotics (rate adjusted for wound classification) yields adjusted infection rates of 5.2 per cent for the group not receiving them and 12.2 per cent for the group receiving them, indicating that a small part of the difference between the crude rates, 4.4 and 14.3 per cent, is explained on the basis of a disproportionate number of nonclean cases in the group receiving antibiotics. Adjustment for no other factor, such as age or duration of operation, produces a similarly substantial change in the infection rates of the treated and untreated groups.

Discussion: It is tempting to ascribe the entire difference between the infection rate in those receiving prophylactic antibiotics and the rate in those not receiving them to the selection of patients, with more infection-prone patients in the antibiotic group. The adjusted rates in Table 54, however, are still higher for the antibiotic group. It may be that patient or operative factors that predispose to infection, more subtle than those recorded in this study, are present and are recognized by the surgeon who prescribes prophylactic antibiotics to the more susceptible patients, causing a further selection of poor-risk patients

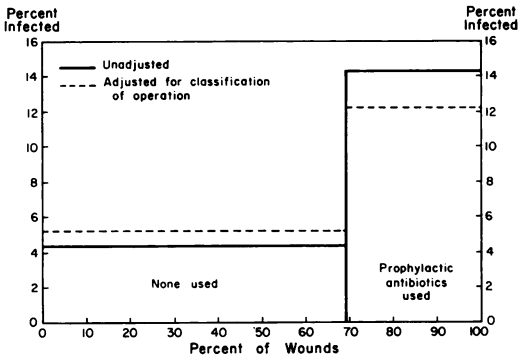

FIG. 32. Percentage of wounds infected, by use of prophylactic antibiotics.

in the treated group. But such factors are not now apparent, and despite the demonstrably biased selection of patients for antibiotic prophylaxis, an effort to correct for the bias does not alter the fact that treated patients have a much higher infection rate than untreated patients. On the basis of the data presented, the possibility that prophylactic antibiotics, as used in this study, may have actually increased the wound infection rate cannot be dismissed.

Nor can firm conclusions be reached with regard to the relative merits of specific antibiotics or antibiotic combinations. When adjusted for wound classification (Table B-38), the infection rates for penicillin alone (5.1%) and for penicillin and tetracycline in combination (5.0%) compare favorably with the adjusted rate of 5.2 per cent for those not receiving antibiotics; however, this comparison is influenced by the fact that the vast majority of patients receiving either of these antibiotic regimens were from Hospital 4, which had the lowest wound infection rate of all the participating hospitals. When these infection rates are adjusted for hospital distribution (Table B-39), both antibiotic regimens demonstrate a higher infection rate than the nontreated group. This wide variation among the participating hospitals in the use of specific antibiotics precludes meaningful comparison of the effectiveness of the different methods of prophylaxis.

In certain specific clinical situations, largely medical, prophylactic antibiotics have been shown to be of value, e.g., the use of penicillin to prevent reactivation of rheumatic heart disease and to prevent ophthalmia neonatorum. In such programs, however, the offending organism, beta-hemolytic streptococcus or gonococcus, is known and is almost uniformly susceptible to the antibiotic used. Such situations are not analogous to the prevention of wound infection in a broad surgical practice.

There is evidence from animal experiments that in certain situations prophylactic antibiotics afford a degree of protection in contaminated wounds (Alexander *et al.*, 1960). On the other hand, Dineen (1960) showed that alteration of the normal intestinal flora of mice with antibiotics actually increased their susceptibility to infection by intravenously administered staphylococci.

Reports of many retrospective clinical studies of the efficacy of prophylactic antibiotics have been published, and most have failed to demonstrate a reduced infection rate in patients so treated. Such studies include those of McKittrick and Wheelock

Table 54. Incidence of Infection, by Use of Prophylactic Antibiotics, Unadjusted and Adjusted for Selected Factors Known to Influence Infection Rates

	Infection rates, percent									
		Adjusted for								
Antibiotic status	Unadjusted	Class of wound	Hospital	Duration of operation	Duration of preoperative hospitalization	Urgency of operation	Diabetes	Steroid therapy	Obesity	Malnutrition
Not used	4.4	5.2	4.6	4.4	4.5	4.5	4.4	4.4	4.4	4.4
Used	14.3	12.2	15.7	13.0	13.9	13.9	14.3	14.3	14.3	14.3
Total	7.4									

(1954) in abdominal surgery, Tachdjian and Compere (1957) in orthopedic surgery, Petersdorf *et al.* (1957) in comatose patients, and Lepper *et al.* (1954) in patients with tracheotomy. Those retrospective studies suffer from the same defect as the present analysis, namely, that the selection of patients to receive antibiotics lay with the responsible physicians, and raise the suspicion of bias and lack of comparability of the treated and nontreated groups. None of the above studies, however, demonstrated a beneficial effect of prophylactic antibiotics.

Two well-controlled prospective studies, involving random selection of treated and control patients, found virtually identical infection rates in the treated and control groups. These were the studies of Appleton and Waisbren (1956), investigating the use of chloramphenicol in transurethral resections of the prostate, and of Sanchez-Ubeda and associates (1958), who used penicillin and dihydrostreptomycin after general surgery. Another prospective study (Johnstone, 1963) revealed a significantly higher infection rate in the treated patients, but the design of his study did not preclude bias in the selection of patients.

On the other hand, Linton (1961) believes that the infection rate following a clean vascular operation is improved by the use of prophylactic antibiotics, although here, too, controlled clinical data are lacking. Kornfield and Allbritten (1961), reviewing their experience with biliary-tract surgery over a five-year period, concluded that antibiotic prophylaxis was beneficial in reducing postoperative infectious complications.

Recently, Ketcham and associates (1962) presented evidence strongly correlating the wound infection rate after radical extirpative cancer surgery with the carrier status of the patients; a high percentage of those who harbored coagulase-positive staphylococci in the anterior nares preoperatively developed postoperative wound infection, usually with a staphylococcus of the identical phage type. Receiving chloramphenicol in high doses (2 Gm./6 hr.) for 10 days postoperatively, these workers found infection rates of 14 per cent in the antibiotic-treated group and 54 per cent in the placebo-treated group, with an impressive corresponding reduction in infection rate in the staphylococcal carriers so treated. In an extension of their former study, Ketcham and co-workers (1963) showed that the same dose of chloromycetin for three days preoperatively and seven days postoperatively was even more effective than 10 days of postoperative treatment, and attributed this to the concomitant reduction in nasal carriers at the time of operation.

If observations of Ketcham and co-workers and those of Williams *et al.* (1959) are correct, that autogenous infection of the staphylococcal nasal carrier is responsible for a large proportion of wound infections, some of the apparent discrepancies between the views previously presented might be resolved. Many reports indicate that penicillin-resistant staphylococcus is the most common single wound pathogen (Williams *et al.*, 1959; Dineen and Pearce, 1958; Howe, 1957; Sanchez-Ubeda *et al.*, 1958). If so, prophylactic antibiotic therapy of penicillin, or of penicillin and streptomycin in combination, should not be expected to reduce the wound infection rate from this organism. Moreover, the work of Knight and co-workers (1954, 1958) and of Dowling, Lepper, and Jackson (1955) indicates that treatment of hospitalized patients with penicillin or tetracycline rapidly induces nasal colonization by antibiotic-resistant staphylococci. It is possible that the routine administration of antibiotics, ineffective against the prevalent drug-resistant staphylococci, may indeed increase the wound infection rate by promoting nasal colonization by these organisms.

In the present study, a higher infection rate was found in those patients who re-

ceived prophylactic antibiotics than in those who did not. For every patient or operative factor known to influence infection rate, the more susceptible patients received antibiotics oftener than the less susceptible. However, even when this bias is statistically corrected for, the group receiving prophylactic antibiotics still has a higher infection rate. Although possible explanations for this finding have been discussed, conclusions must be limited to the negative observation that no benefit from the use of prophylactic antibiotics could be demonstrated.

Summary of Clinical Observations

The foregoing has concerned the various factors influencing the incidence of wound infection in a cooperative study among five hospitals over a two-year period that involved 14,854 operations and 15,613 incisions. The double-blind principle was used to investigate the efficacy of ultraviolet irradiation of the operating rooms, in which ultraviolet and dummy lamps were alternated on a predetermined, randomized basis.

Ultraviolet irradiation did achieve an impressive reduction in the number of airborne bacteria in the operating room; however, the wound infection rate following operation in irradiated rooms was 7.4 per cent, hardly lower than the rate of 7.5 per cent following operation in control rooms (rooms with dummy lamps). The only wounds to show a statistically significant benefit from the use of ultraviolet radiation were refined-clean wounds, whose rate was reduced from 3.8 to 2.9 per cent. This beneficial effect of ultraviolet irradiation, confined to refined-clean wounds (which represented only 19.2 per cent of all the infections in the study), was lost in the over-all operative experience, offset by an apparent detrimental effect of irradiation in nonclean wounds.

The *over-all incidence of infection at each of the five participating hospitals* varied from a low of 3.0 per cent to a high of 11.7 per cent. Neither patient selection nor type of operation performed accounts for this wide variation. It is believed that the carefully formulated, objective definition of wound infection used throughout the study prevented major discrepancies in this area from occurring among hospitals, and that the infection rate reported for each institution closely approximates the true incidence of infection. The striking differences in infection rates at different hospitals cannot be easily explained by retrospective analysis, but are intriguing subjects for conjecture.

The *incidence of wound infection following a number of frequently performed operative procedures* has been tabulated and possible explanations for the differences offered. The risk of wound infection following a specific procedure may be regarded as dependent on not one but many interacting factors, including bacterial, patient, and operative characteristics.

The *degree of bacterial contamination* of each wound was assessed clinically at the time of operation and the procedure classified accordingly. The following infection rates for the five categories of operations were found: refined-clean wounds, 3.3 per cent; other clean wounds, 7.4 per cent; clean-contaminated wounds, 10.8 per cent; contaminated wounds, 16.3 per cent; and dirty wounds, 28.6 per cent. The relationship of infection rate to degree of bacterial contamination appears to be independent of the other factors that influence the wound infection rate.

Certain patient characteristics were recorded at the time of operation and have been examined with respect to their relationship to wound infection rate. They are summarized below.

The *age* of the patient appears to exert a direct influence on wound infection rate, which rises steadily from 4.7 per cent in the 15- to 24-year-old group to 10.7 per cent in the 65- to 74-year-old group. The

relationship of risk of sepsis to age appears to be at least partially independent of other factors that influence infection rate.

The *sex* of the patient was found to be only indirectly related to the risk of infection. The over-all infection rate in males was 8.0 per cent, significantly higher than that in females, 6.9 per cent. The difference is explained on the basis of a greater proportion of contaminated cases in the male population. When this disproportion is corrected for, the adjusted infection rate in males is found to be 7.6 per cent, and that in females, 7.3 per cent, indicating that for operations in which a similar degree of bacterial contamination can be expected to occur there is virtually no difference in the risk of infection between sexes.

The *race* of the patient played at most a minor role as a determinant of wound infection rate. Although the infection rate in whites, 7.6 per cent, was higher than in nonwhites, 6.8 per cent, the difference was the result of a disproportionate concentration of nonwhites at the hospital with the lowest infection rate. Correction for hospital distribution yielded adjusted infection rates of 7.1 per cent in whites and 8.6 per cent in nonwhites.

The presence of *diabetes* was associated with an infection rate of 10.4 per cent, in contrast with a rate of 7.3 per cent in those without diabetes. The difference appears to result from the heavy concentration of older patients in the diabetic group. When infection rates are adjusted for age, the rate for diabetics becomes 7.2 per cent, and that for nondiabetics, 7.4 per cent. This indicates that in the present series diabetics showed no increased susceptibility to infection when compared with nondiabetics of similar ages.

Steroid therapy affected the wound infection rate adversely, with 16.0 per cent of the wounds in patients receiving such treatment becoming infected and only 7.3 per cent in those not receiving steroids. The patients treated with steroids on the average were older, had longer operations, stayed in the hospital longer preoperatively, and were concentrated to some extent in hospitals with higher over-all infection rates. Although each of these associated factors tended to raise the infection rate in the steroid-treated group, steroid therapy itself may have increased those patients susceptibility to infection.

Patients characterized as *extremely obese* manifested a wound infection rate of 18.1 per cent, and those not so described, a rate of 7.3 per cent. Although the obese patients tended to have slightly longer operations, adjustment for that factor did not greatly diminish the startling infection rate in them, and obesity itself appears to have a major, direct influence on wound infection rate.

Patients with *severe malnutrition* displayed an infection rate of 22.4 per cent, and those without this condition, a rate of 7.3 per cent. The remarkably high infection rate in the malnourished is, however, artificially distorted by a number of associated factors. The malnourished patients in general were older, had longer operations, and had more contaminated wounds than the average. In addition, more than half of them were operated on at the institution with the highest over-all infection rate. Correction for each of these factors individually greatly lowered the infection rates for the malnourished patients, e.g., to 9.3 per cent when adjusted for hospital distribution and 13.7 per cent when adjusted for wound classification. The reductions are of such magnitude as to cast doubt on the widely held belief that the malnourished patient is intrinsically more susceptible to infection than a patient of normal nutritional status undergoing a comparable operative procedure.

Patients who harbored *infection remote from the operative incision* were found to have a wound infection rate of 18.4 per cent, and those without such remote infection, a rate of 6.7 per cent. Although the

way in which patient susceptibility to wound infection is increased by the presence of remote infection is not clear, it is apparent that the effect is direct, unexplained by the other associated factors predisposing the patient to infection, and of considerable magnitude.

Two features of the operative wound were examined in relation to wound infection rate: the type of closure employed and the use of drains. Because of the different operative situations associated with the use of different types of wound closure and drains, only limited conclusions could be drawn from the data obtained.

The *type of wound closure* used by the surgeon influenced the infection rate for the most part indirectly, insofar as the two largest categories of wound closure were concerned; although 7.0 per cent of wounds closed primarily became infected, 15.2 per cent of those not closed or incompletely closed became infected. The difference appears to result from the greater proportion of nonclean operations in the group without primary closure. When adjusted for wound classification, the infection rates become 10.0 per cent for wounds closed primarily and 11.9 per cent for wounds incompletely closed or left open. Secondary wound closure was associated with an infection rate of 28.2 per cent, and skin graft closure, a rate of 17.2 per cent.

The use of a *drain* was associated with an infection rate of 11.1 per cent, and undrained wounds, a rate of 5.0 per cent. The depth or site of exit of the drain did not alter the infection rates in drained wounds to an appreciable degree; infection rates of 11.5, 12.0, and 11.3 per cent were observed for subcutaneous drains brought out through the incision, for drains from serous cavities brought out through the incision, and for drains brought out through separate stab wounds, respectively. The higher infection rate in drained wounds cannot be explained on the basis of any other associated factor recorded in the study that might increase the infection rate in patients with drained wounds. Nevertheless, in view of objective and subjective criteria for surgical drainage at the time of wound closure, it is believed that the drained and undrained wounds are not comparable in all other respects, and it cannot be concluded that the drains themselves were responsible for the higher infection rate.

Duration of operation exerted a profound and direct influence on wound infection rate, with the incidence of wound infection rising steadily from 3.6 per cent after procedures lasting less than 30 minutes to 18.0 per cent after those lasting over 6 hours. This striking association is independent of other factors that influence wound infection rate, and appears to be a primary determinant of the risk of infection.

Urgency of operation only indirectly influenced wound infection rate. Although urgent operations were found to be associated with an 11.7-per cent wound infection rate, emergency procedures with a 12.1-per cent rate, and elective procedures with only a 6.7 per cent rate, the differences are explained entirely by the preponderance of nonclean procedures in the nonelective group. When adjusted for degree of operative bacterial contamination (as defined by wound classification), the infection rates for elective, urgent, and emergency procedures are virtually the same: 10.9, 10.7, and 10.2 per cent, respectively.

The *time of day* when the operation was performed did not exert a substantial direct effect on wound infection rate. Although the incidence of wound infection rose from 6.5 per cent in procedures started between 7:30 and 9:30 a.m. to 10.9 per cent in those started between 3:30 p.m. and midnight, the increase reflects the greater proportion of nonclean and nonelective operations in the later hours. The infection rate for all clean cases was virtually constant throughout the day.

No definite *seasonal trend* in infection

rate could be identified when infections were grouped according to the *month of operation.* Although there was considerable random variation in some subgroups of the total experience, no convincing evidence for a seasonal concentration of infections could be found.

Duration of preoperative hospitalization was found to be closely related to the incidence of wound infection. Patients hospitalized fewer than two days preoperatively had a wound infection rate of 6.0 per cent, and those hospitalized longer than three weeks preoperatively, a rate of 14.7 per cent. The relationship cannot be explained on the basis of other associated factors recognized in the study as increasing infection rate. It appears that the duration of preoperative hospitalization, or factors correlated with it but not identified in this study, markedly influences the infection rate independently of the various patient and operative factors studied here.

The use of *prophylactic antibiotics* is paradoxically associated with a much higher wound infection rate, 14.3 per cent, than that for patients not receiving prophylactic antibiotics, 4.4 per cent. Although the patients with increased susceptibility to infection received prophylactic antibiotics much more frequently than other patients, adjustment for all recognizable factors involved in this bias does not change the finding that patients who received antibiotics to prevent wound infection actually manifested an increased wound infection rate. Whether this finding represents fact or artifact can be determined only by carefully controlled studies in which the use of prophylactic antibiotics is randomized and not determined, as in the present study, by the clinical judgment of the surgeon.